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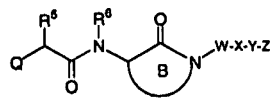
(54) Title: SUBSTITUTED LACTAMS AS INHIBITORS OF Aβ PROTEIN PRODUCTION



(I)

(57) Abstract: This invention relates to novel lactams of Formula (I) having drug and bio-affecting properties, their pharmaceutical compositions and methods of use. These novel compounds inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurological deposits of amyloid protein. More particularly, the present invention relates to the treatment of neurological disorders related to β-amyloid production such as Alzheimer's disease and Down's Syndrome.

TITLE

SUBSTITUTED LACTAMS AS INHIBITORS OF Aβ PROTEIN PRODUCTION

FIELD OF THE INVENTION

This invention relates to novel lactams having drug and bio-affecting properties, their pharmaceutical compositions and methods of use. These novel compounds inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurological deposits of amyloid protein. More particularly, the present invention relates to the treatment of neurological disorders related to β-amyloid production such as Alzheimer's disease and Down's Syndrome.

BACKGROUND OF THE INVENTION

Alzheimer's disease (AD) is a degenerative brain disorder characterized clinically by progressive loss of memory, temporal and local orientation, cognition, reasoning, judgment and emotionally stability. AD is a common cause of progressive dementia in humans and is one of the major causes of death in the United States. AD has been observed in all races and ethnic groups worldwide, and is a major present and future health problem. No treatment that effectively prevents AD or reverses the clinical symptoms and underlying pathophysiology is currently available (for review see Dennis J. Selkoe; Cell Biology of the amyloid (beta)-protein precursor and the mechanism of Alzheimer's disease, Annu Rev Cell Biol, 1994, 10: 373-403).

Histopathological examination of brain tissue derived upon autopsy or from neurosurgical specimens in effected individuals revealed the occurrence of amyloid plaques and neurofibrillar tangles in the cerebral cortex of such patients. Similar alterations were observed in patients with Trisomy 21 (Down's syndrome), and hereditary cerebral hemorrhage with amyloidosis of the Dutch-type.

Neurofibrillar tangles are nonmembrane-bound bundles of abnormal proteinaceous filaments and biochemical and immunochemical studies led to the conclusion that their principle protein subunit is an altered phosphorylated form of the tau protein (reviewed in Selkoe, 1994).

Biochemical and immunological studies revealed that the dominant proteinaceous component of the amyloid plaque is an approximately 4.2 kilodalton (kD) protein of about 39 to 43 amino acids. This protein was designated Aβ, β-amyloid peptide, and sometimes β/A4; referred to herein as Aβ. In addition to its deposition in amyloid plaques, Aβ is also found in the walls of meningeal and parenchymal arterioles, small arteries, capillaries, and sometimes, venules. Aβ was first purified and a partial amino acid reported in 1984 (Glenner and Wong, Biochem. Biophys. Res. Commun. 120: 885-890). The isolation and sequence data for the first 28 amino acids are described in U.S. Pat. No 4,666,829.

Compelling evidence accumulated during the last decade revealed that Aβ is an internal polypeptide derived from a type 1 integral membrane protein, termed β amyloid precursor protein (APP). β APP is normally produced by many cells both in vivo and in cultured cells, derived from various animals and humans. Aβ is derived from cleavage of β APP by as yet unknown enzyme (protease) system(s), collectively termed secretases.

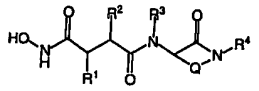
The existence of at least four proteolytic activities has been postulated. They include β secretase(s), generating the N-terminus of Aβ, α secretase(s) cleaving around the 16/17 peptide bond in Aβ, and γ secretases, generating C-terminal Aβ fragments ending at position 38, 39, 40, 42, and 43 or generating C-terminal extended precursors which are subsequently truncated to the above polypeptides.

Several lines of evidence suggest that abnormal accumulation of Aβ plays a key role in the pathogenesis of AD. Firstly, Aβ is the major protein found in amyloid

plaques. Secondly, Aβ is neurotoxic and may be causally related to neuronal death observed in AD patients. Thirdly, missense DNA mutations at position 717 in the 770 isoform of β APP can be found in effected members but not unaffected members of several families with a genetically determined (familiar) form of AD. In addition, several other β APP mutations have been described in familiar forms of AD. Fourthly, similar neuropathological changes have been observed in transgenic animals overexpressing mutant forms of human β APP. Fifthly, individuals with Down's syndrome have an increased gene dosage of β APP and develop early-onset AD. Taken together, these observations strongly suggest that Aβ depositions may be causally related to the AD.

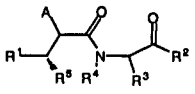
It is hypothesized that inhibiting the production of Aβ will prevent and reduce neurological degeneration, by controlling the formation of amyloid plaques, reducing neurotoxicity and, generally, mediating the pathology associated with Aβ production. One method of treatment methods would therefore be based on drugs that inhibit the formation of Aβ in vivo. Methods of treatment could target the formation of Aβ through the enzymes involved in the proteolytic processing of β amyloid precursor protein. Compounds that inhibit β or γsecretase activity, either directly or indirectly, could control the production of Aβ. Advantageously, compounds that specifically target γ secretases, could control the production of Aβ. Such inhibition of β or γsecretases could thereby reduce production of Aβ, which, thereby, could reduce or prevent the neurological disorders associated with Aβ protein.

PCT publication number WO 96/29313 discloses the general formula:

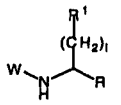


covering metalloprotease inhibiting compounds useful for the treatment of diseases associated with excess and/or unwanted matrix metalloprotease activity, particularly collagenase and or stromelysin activity.

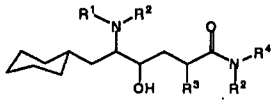
Compounds of general formula:



are disclosed in PCT publication number WO 95/22966 relating to matrix metalloprotease inhibitors. The compounds of the invention are useful for the treatment of conditions associated with the destruction of cartilage, including corneal ulceration, osteoporosis, periodontitis and cancer. European Patent Application number EP 0652009A1 relates to the general formula:



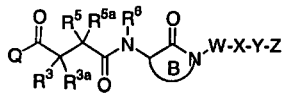
and discloses compounds that are protease inhibitors that inhibit Aβ production. US Patent Number 5703129 discloses the general formula:



which covers 5-amino-6-cyclohexyl-4-hydroxy-hexanamide derivatives that inhibit Aβ production and are useful in the treatment of Alzheimer's disease.

Copending, commonly assigned U.S. patent application Serial Number 09/370089 filed August 7, 1999 (equivalent to

international application PCT US99/17717) discloses lactams of general formula:



wherein the lactam ring B is substituted by succinamide and a carbocyclic, aryl, or heteroaryl group. These compounds inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurological deposits of amyloid protein.

None of the above references teaches or suggests the compounds of the present invention which are described in detail below.

SUMMARY OF THE INVENTION

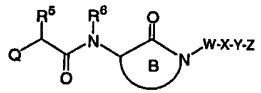
One object of the present invention is to provide novel compounds which are useful as inhibitors of the production of Aβ protein or pharmaceutically acceptable salts or prodrugs thereof.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide a method for treating degenerative neurological disorders comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

These and other objects, which will become apparent during the following detailed description, have been

achieved by the inventors' discovery that compounds of Formula (I):

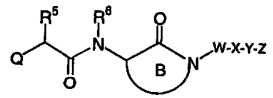


(I)

or pharmaceutically acceptable salt or prodrug forms thereof, wherein Q, R^5, R^6, W, X, Y, Z, and ring B are defined below, are effective inhibitors of the production of Aβ.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[1] Thus, in a first embodiment, the present invention provides a novel compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-S-R^4$,
$-(CR^7R^{7a})_n-O-R^4$,
$-(CR^7R^{7a})_m-N(R^{7b})-R^4$,
$-(CR^7R^{7a})_n-S(=O)-R^4$,
$-(CR^7R^{7a})_n-S(=O)_2-R^4$, or
$-(CR^7R^{7a})_n-C(=O)-R^4$;
provided when n is 0, then R^4 is not H;

m is 1, 2, or 3;

n is 0, 1, or 2;

R^4 is H,
C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, OR^{14a}, OR^{22}, SR^{22}, $C(=O)OR^{22}$, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from: H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3 R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, aryl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^7, at each occurrence, is independently H or C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently H or C_1-C_4 alkyl;

R^{7b} is H or C_1-C_4 alkyl;

Ring B is a 7 membered lactam,
wherein the lactam is saturated, partially saturated or unsaturated;
wherein each additional lactam carbon is substituted with 0-2 R^{11}; and,
optionally, the lactam contains a heteroatom selected from -O-, -S-, -S(=O)-, $-S(=O)_2-$, -N=, -NH-, and -$N(R^{10})$-;

additionally, two R^{11} substituents on adjacent atoms may be combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{13};

additionally, two R^{11} substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R^{13};

additionally, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle substituted with 0-3 R^{13};

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl optionally substituted with 0-3 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{11}, at each occurrence, is independently selected from H, C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with 0-3 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3;
phenyl substituted with 0-3 R^{11b};
C_3-C_6 cycloalkyl substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

W is a bond or $-(CR^8R^{8a})_p-$;

p is 0, 1, 2, 3, or 4;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;
C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

Y is a bond or $-(CR^9R^{9a})_t$-V-$(CR^9R^{9a})_u-$;

t is 0, 1, or 2;

u is 0, 1, or 2;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, -C(=O)-, -O-, -S-, -S(=O)-, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, -C(=O)O-, or -OC(=O)-;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a};
C_2-C_6 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_6-C_{10} aryl substituted with 0-4 R^{12b}; C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, aryl, C_3-C_6 cycloalkyl, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from

H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-7 membered ring wherein said 4-7 membered ring optionally contains an additional heteroatom selected from O or NH;

R^{17} is H, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or $-CH_2$-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF_3, OCF_3, SCH_3, $S(O)CH_3$, SO_2CH_3, $-NH_2$, $-N(CH_3)_2$, or C_1-C_4 haloalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19b}, at each occurrence, is independently is H or C_1-C_4 alkyl;

R^{21} is H, phenyl, benzyl, or C_1-C_4 alkyl; and

R^{22} is C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_3-C_4 alkynyl.

[2] In a preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein :

Q is $-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-S-R^4$,
$-(CR^7R^{7a})_n-O-R^4$, or
$-(CR^7R^{7a})_m-N(R^{7b})-R^4$;

m is 1 or 2;

n is 0 or 1;

R^4 is H,
C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, OR^{14a}, $C(=O)OR^{22}$, SR^{22}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

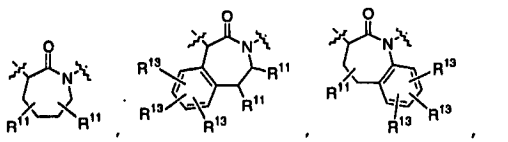
R^6 is H, methyl, or ethyl;

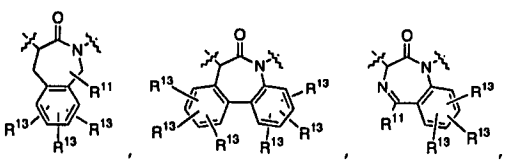
R^7, at each occurrence, is independently H or C_1-C_4 alkyl;

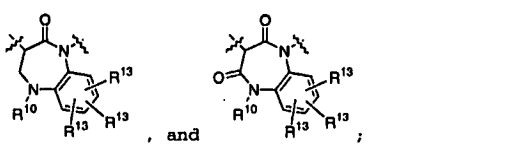
R^{7a}, at each occurrence, is independently H or C_1-C_4 alkyl;

R^{7b} is H or C_1-C_4 alkyl;

Ring B is selected from:







, and ;

R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl optionally substituted with 0-3 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3,

$S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{11}, at each occurrence, is independently selected from H, C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with 0-3 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3;
phenyl substituted with 0-3 R^{11b};
C_3-C_6 cycloalkyl substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

W is a bond or $-(CH_2)_p-$;

p is 1 or 2;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 carbocycle substituted with 0-2 R^{Xb}; or

5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, and C_1-C_3 halothioalkoxy;

Y is a bond, -C(=O)-, -O-, -S-, -S(=O)-, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, -C(=O)O-, or -OC(=O)-;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a};
C_2-C_6 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_6-C_{10} aryl substituted with 0-4 R^{12b}; C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-7 membered ring wherein said 4-7 membered ring optionally contains an additional heteroatom selected from O or NH;

R^{17} is H, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or $-CH_2$-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF_3, OCF_3, SCH_3, $S(O)CH_3$, SO_2CH_3, $-NH_2$, $-N(CH_3)_2$, or C_1-C_4 haloalkyl;

R^{18}, at each occurrence, is independently selected from

H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

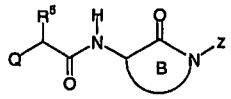
R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenethyl;

R^{19b}, at each occurrence, is independently is H or C_1-C_4 alkyl;

R^{21} is H, phenyl, benzyl, or C_1-C_4 alkyl; and

R^{22} is C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_3-C_4 alkynyl.

[3] In another preferred embodiment, the present invention provides for a compound of Formula (Ib),



(Ib)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CHR^7)_m-R^4$,
$-(CHR^7)_n-S-R^4$,
$-(CHR^7)_n-O-R^4$, or
$-(CHR^7)_m-N(R^{7b})-R^4$;

m is 1 or 2;

n is 0 or 1;

R^4 is H,
C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},

C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, OR^{14a}, $C(=O)OR^{22}$, SR^{22}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

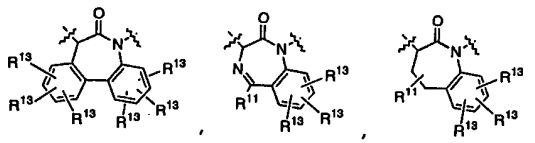
R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $R^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

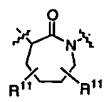
R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^7, at each occurrence, is independently H, methyl, or ethyl;

R^{7b} is H, methyl, or ethyl;

Ring B is selected from:





and ;

R^{11}, at each occurrence, is independently selected from
H, C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with 0-3 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};

C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3;
phenyl substituted with 0-3 R^{11b};
C_3-C_6 cycloalkyl substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

W is a bond;
X is a bond;
Y is a bond;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a};
C_2-C_6 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_6-C_{10} aryl substituted with 0-4 R^{12b}; C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-7

membered ring wherein said 4-7 membered ring optionally contains an additional heteroatom selected from O or NH;

R^{17} is H, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or $-CH_2$-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF_3, OCF_3, SCH_3, $S(O)CH_3$, SO_2CH_3, $-NH_2$, $-N(CH_3)_2$, or C_1-C_4 haloalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenethyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

[4] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CH_2)_m-R^4$, $-(CH_2)_n-S-R^4$, $-(CH_2)_n-O-R^4$, or $-(CH_2)_m-N(H)-R^4$;

m is 1 or 2;

n is 0 or 1;

R^4 is C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{22}, OR^{14a}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

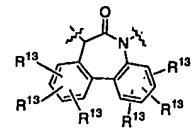
R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};

C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from: H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $R^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

Ring B is selected from: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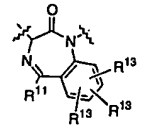
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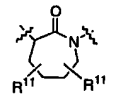
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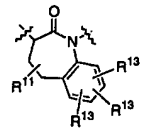

;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;

C_1-C_4 alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, Cl, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond;
X is a bond;
Y is a bond;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a}; or
C_2-C_6 alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_6-C_{10} aryl substituted with 0-4 R^{12b};

C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b}; and wherein said 5 to 10 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl;

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-; and

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-6 membered ring wherein said 4-6 membered ring optionally contains an additional heteroatom selected from O or NH, wherein said 4-6 membered ring is selected from imidazolidinyl, oxazolidinyl, thiazolidinyl, piperazinyl, morpholinyl, and thiomorpholinyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenethyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

[5] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-3 R^{4a},
C_2-C_6 alkenyl substituted with 0-3 R^{4a},
C_2-C_6 alkynyl substituted with 0-3 R^{4a},
C_3-C_6 carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{14a}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

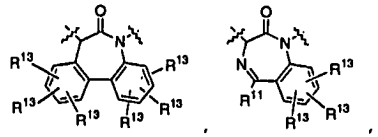
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

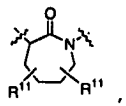
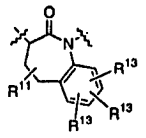
R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b}; or
C_2-C_6 alkynyl substituted with 0-3 R^{5b};

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, Cl, F, Br, I, =O;
C_3-C_6 carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Ring B is selected from:



R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;
C_1-C_4 alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, methoxy, ethoxy,

propoxy, phenoxy, F, Cl, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond;
X is a bond;
Y is a bond;

Z is H;
C_1-C_4 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a}; or
C_2-C_4 alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, and benzyl;

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-$S(=O)_2$-, and ethyl-$S(=O)_2$-;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl;

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

[6] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-2 R^{4a},
C_2-C_6 alkenyl substituted with 0-2 R^{4a},
C_2-C_6 alkynyl substituted with 0-2 R^{4a}, or
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, OH, F, Cl, Br, I, CN, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, methoxy, ethoxy, propoxy, OCF_3;
C_3-C_6 carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl,

thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

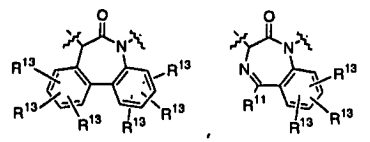
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

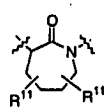
R^5 is H;
C_1-C_4 alkyl substituted with 0-1 R^{5b};
C_2-C_4 alkenyl substituted with 0-1 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-1 R^{5b};

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3;
C_3-C_6 carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Ring B is selected from:

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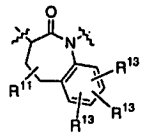

;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$;
C_1-C_4 alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, methoxy, ethoxy, propoxy, phenoxy, F, Cl, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond;
X is a bond;

Y is a bond;

Z is H;
C_1-C_4 alkyl substituted with 0-1 R^{12a};
C_2-C_4 alkenyl substituted with 0-1 R^{12a}; or
C_2-C_4 alkynyl substituted with 0-1 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R^{15}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl; and

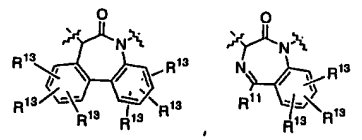
R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, and phenethyl;

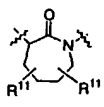
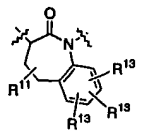
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl.

[7] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Ring B is selected from:



, and ;

R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2NH_2$, $-CH_2N(CH_3)_2$, $-CH_2N(CH_2CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, or $-CH_2CH_2$-cyclohexyl;

Q is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, $-CH_2CH_2$-cyclohexyl, $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$, $-OCH(CH_3)_2$, $-OCH_2CH_2CH_2CH_3$, $-OCH_2CH(CH_3)_2$, $-OCH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH(CH_3)_2$, $-OCH_2$-cyclopropyl, $-OCH_2$-cyclobutyl, $-OCH_2$-cyclopentyl, $-OCH_2$-cyclohexyl, $-OCH_2CH_2$-cyclopropyl, $-OCH_2CH_2$-cyclobutyl,

$-OCH_2CH_2$-cyclopentyl, $-OCH_2CH_2$-cyclohexyl, $-CH_2OCH_2CH_3$, $-CH_2OCH_2CH_2CH_3$, $-CH_2$-$OCH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH(CH_3)_2$, $-CH_2O$-cyclopropyl, $-CH_2O$-cyclobutyl, $-CH_2O$-cyclopentyl, $-CH_2O$-cyclohexyl, $-CH_2OCH_2$-cyclopropyl, $-CH_2OCH_2$-cyclobutyl, $-CH_2OCH_2$-cyclopentyl, $-CH_2OCH_2$-cyclohexyl; $-CH_2(NH)CH_3$, $-CH_2(NH)CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH_3$, $-CH_2$-$(NH)CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)$-cyclopropyl, $-CH_2(NH)$-cyclobutyl, $-CH_2(NH)$-cyclopentyl, $-CH_2(NH)$-cyclohexyl, $-CH_2(NH)CH_2$-cyclopropyl, $-CH_2(NH)CH_2$-cyclobutyl, $-CH_2(NH)CH_2$-cyclopentyl, or $-CH_2(NH)CH_2$-cyclohexyl;

W is a bond;
X is a bond;
Y is a bond;

Z is methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl, s-butyl, t-butyl, or allyl;

R^{11}, at each occurrence, is independently selected from H, =O, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 3-F-phenyl, (3-F-phenyl)CH_2-, (3-F-phenyl)CH_2CH_2-, 2-F-phenyl, (2-F-phenyl)CH_2-, (2-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 3-Cl-phenyl, (3-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 3-CH_3-phenyl, (3-CH_3-phenyl)CH_2-, (3-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, (4-CF_3-phenyl)CH_2CH_2-, pyrid-2-yl, 4-F-pyrid-2-yl, 4-Cl-pyrid-2-yl, 4-CH_3-pyrid-2-yl, 4-CF_3-pyrid-2-yl, pyrid-3-yl,

4-F-pyrid-3-yl, 4-Cl-pyrid-3-yl, 4-CH_3-pyrid-3-yl, 4-CF_3-pyrid-3-yl, or pyrid-4-yl; and

R^{13}, at each occurrence, is independently selected from H, F, Cl, OH, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, or $-CF_3$.

[8] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CH_2)_m-R^4$,
$-(CH_2)_n-S-R^4$,
$-(CH_2)_n-O-R^4$, or
$-(CH_2)_m-N(H)-R^4$;

m is 1 or 2;

n is 0 or 1;

R^4 is C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{22}, OR^{14a}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, and

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

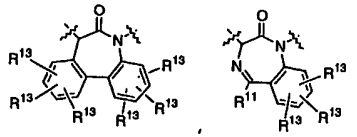
R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

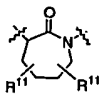
R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and

C_1-C_4 haloalkoxy;

Ring B is selected from:

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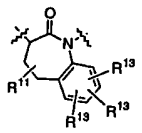

;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;
C_1-C_4 alkyl optionally substituted with 0-3 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; and wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_4 haloalkoxy;

W is a bond, $-CH_2-$, $-CH_2CH_2-$;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-2 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is C_1-C_3 alkyl substituted with 1-2 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl; or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-; and

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-6 membered ring wherein said 4-6 membered ring optionally contains an additional heteroatom selected from O or NH, wherein said 4-6 membered ring is selected from imidazolidinyl, oxazolidinyl, thiazolidinyl, piperazinyl, morpholinyl, and thiomorpholinyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

[9] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-3 R^{4a};
C_2-C_6 alkenyl substituted with 0-3 R^{4a};
C_2-C_6 alkynyl substituted with 0-3 R^{4a};
C_3-C_6 carbocycle substituted with 0-3 R^{4b};
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{14a}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

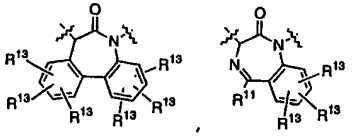
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

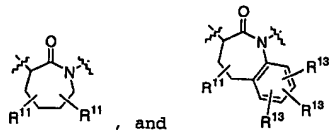
R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b}; or
C_2-C_6 alkynyl substituted with 0-3 R^{5b};

R^{5b}, at each occurrence, is independently selected from: H, methyl, ethyl, propyl, butyl, CF_3, Cl, F, Br, I, =O;
C_3-C_6 carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Ring B is selected from:





R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;
C_1-C_4 alkyl optionally substituted with 0-3 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; and wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, phenoxy, Cl, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_4 haloalkoxy;

W is a bond, $-CH_2-$, $-CH_2CH_2-$;

X is a bond;
phenyl substituted with 0-1 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-1 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-1 R^{Xb};

R^{Xb} is selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, methoxy, ethoxy, propoxy, and $-OCF_3$;

Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, or $-N(CH_2CH_3)-$;

Z is C_1-C_2 alkyl substituted with 1-2 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, and benzyl;

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-$S(=O)_2$-, and ethyl-$S(=O)_2$-;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl;

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl; and

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

[10] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-2 R^{4a},
C_2-C_6 alkenyl substituted with 0-2 R^{4a},
C_2-C_6 alkynyl substituted with 0-2 R^{4a}, or
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, OH, F, Cl, Br, I, CN, $NR^{15}NR^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, OCF_3;

C_3-C_6 carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

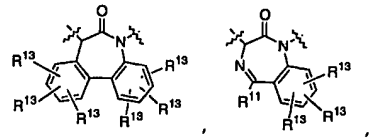
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

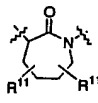
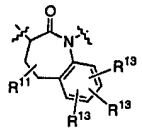
R^5 is H;
C_1-C_4 alkyl substituted with 0-1 R^{5b};
C_2-C_4 alkenyl substituted with 0-1 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-1 R^{5b};

R^{5b}, at each occurrence, is independently selected from: H, methyl, ethyl, propyl, butyl, CF_3;
C_3-C_6 carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Ring B is selected from:



, and ;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$;
C_1-C_4 alkyl optionally substituted with 0-3 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; and wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, phenoxy, Cl, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond or $-CH_2-$;

X is a bond;
phenyl substituted with 0-1 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-1 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-1 R^{Xb};

R^{Xb} is selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, methyl, ethyl, methoxy, ethoxy, and $-OCF_3$;

Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, or $-N(CH_2CH_3)-$;

Z is C_1-C_2 alkyl substituted with 1-2 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b}; and wherein said 5 to 10 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrazolyl,

imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl;

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, and $-OCF_3$;

R^{13}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R^{15}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl; and

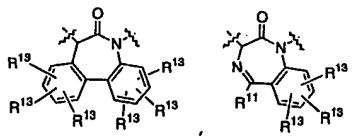
R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, and phenethyl;

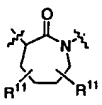
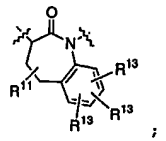
R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl.

[11] In another preferred embodiment, the present invention provides for a compound of Formula (I), or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Ring B is selected from:



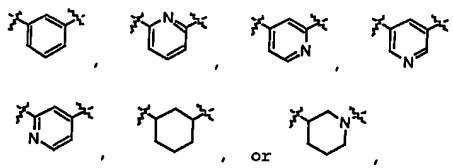
R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2NH_2$, $-CH_2N(CH_3)_2$, $-CH_2N(CH_2CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, or $-CH_2CH_2$-cyclohexyl;

Q is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, $-CH_2CH_2$-cyclohexyl, $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$, $-OCH(CH_3)_2$, $-OCH_2CH_2CH_2CH_3$, $-OCH_2CH(CH_3)_2$, $-OCH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH(CH_3)_2$, $-OCH_2$-cyclopropyl, $-OCH_2$-cyclobutyl, $-OCH_2$-cyclopentyl, $-OCH_2$-cyclohexyl, $-OCH_2CH_2$-cyclopropyl, $-OCH_2CH_2$-cyclobutyl, $-OCH_2CH_2$-cyclopentyl, $-OCH_2CH_2$-cyclohexyl,

$-CH_2OCH_2CH_3$, $-CH_2OCH_2CH_2CH_3$, $-CH_2-OCH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH(CH_3)_2$, $-CH_2O$-cyclopropyl, $-CH_2O$-cyclobutyl, $-CH_2O$-cyclopentyl, $-CH_2O$-cyclohexyl, $-CH_2OCH_2$-cyclopropyl, $-CH_2OCH_2$-cyclobutyl, $-CH_2OCH_2$-cyclopentyl, $-CH_2OCH_2$-cyclohexyl; $-CH_2(NH)CH_3$, $-CH_2(NH)CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH_3$, $-CH_2-(NH)CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)$-cyclopropyl, $-CH_2(NH)$-cyclobutyl, $-CH_2(NH)$-cyclopentyl, $-CH_2(NH)$-cyclohexyl, $-CH_2(NH)CH_2$-cyclopropyl, $-CH_2(NH)CH_2$-cyclobutyl, $-CH_2(NH)CH_2$-cyclopentyl, or $-CH_2(NH)CH_2$-cyclohexyl;

W is a bond or $-CH_2-$;

X is a bond;



Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, or $-N(CH_3)-$,

Z is phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl, 2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl, 2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl, 3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl, 2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl, 3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl, 3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl,

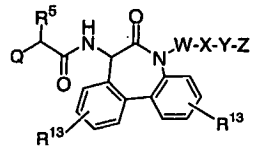
3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl, 4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl, 2-CF_3O-phenyl, 3-CF_3O-phenyl, 4-CF_3O-phenyl, furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl, 4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl, 1-benzimidazolyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, N-piperinyl, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-, (3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, (2-MeO-phenyl)CH_2-, (3-MeO-phenyl)CH_2-, (4-MeO-phenyl)CH_2-, (2-Me-phenyl)CH_2-, (3-Me-phenyl)CH_2-, (4-Me-phenyl)CH_2-, (2-MeS-phenyl)CH_2-, (3-MeS-phenyl)CH_2-, 4-MeS-phenyl)CH_2-, (2-CF_3O-phenyl)CH_2-, (3-CF_3O-phenyl)CH_2-, (4-CF_3O-phenyl)CH_2-, (furanyl)CH_2-, (thienyl)CH_2-, (pyridyl)CH_2-, (2-Me-pyridyl)CH_2-, (3-Me-pyridyl)CH_2-, (4-Me-pyridyl)CH_2-, (1-imidazolyl)CH_2-, (oxazolyl)CH_2-, (isoxazolyl)CH_2-, (1-benzimidazolyl)CH_2-, (cyclopropyl)CH_2-, (cyclobutyl)CH_2-, (cyclopentyl)CH_2-, (cyclohexyl)CH_2-, (morpholino)CH_2-, (N-pipridinyl)CH_2-, or (phenyl)$_2$CH-;

R^{11}, at each occurrence, is independently selected from H, =O, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 3-F-phenyl, (3-F-phenyl)CH_2-, (3-F-phenyl)CH_2CH_2-, 2-F-phenyl, (2-F-phenyl)CH_2-, (2-F-phenyl)CH_2CH_2-,

4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 3-Cl-phenyl, (3-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 3-CH_3-phenyl, (3-CH_3-phenyl)CH_2-, (3-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, (4-CF_3-phenyl)CH_2CH_2-, pyrid-2-yl, 4-F-pyrid-2-yl, 4-Cl-pyrid-2-yl, 4-CH_3-pyrid-2-yl, 4-CF_3-pyrid-2-yl, pyrid-3-yl, 4-F-pyrid-3-yl, 4-Cl-pyrid-3-yl, 4-CH_3-pyrid-3-yl, 4-CF_3-pyrid-3-yl, or pyrid-4-yl; and

R^{13}, at each occurrence, is independently selected from H, F, Cl, OH, -CH_3, -CH_2CH_3, -OCH_3, or -CF_3.

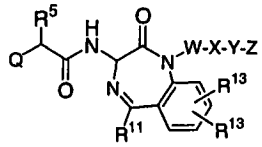
[12] In another preferred embodiment, the present invention provides for a compound of Formula (Ic):



(Ic)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

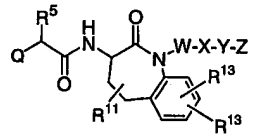
[13] In another preferred embodiment, the present invention provides for a compound of Formula (Id):



(Id)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

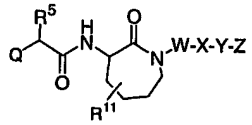
[14] In another preferred embodiment, the present invention provides for a compound of Formula (Ie):



(Ie)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

[15] In another preferred embodiment, the present invention provides for a compound of Formula (If):



(If)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

[16] In another preferred embodiment, the present invention provides for a compound, or a pharmaceutically acceptable salt or prodrug thereof, selected from:

(3S)-3-[(1-oxo-(2S)-2-cyclopropylmethyl-heptyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-propyloctyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-propylnonanyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-butyloctyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-(1-oxo-2-methyloctyl)amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-pentylheptanyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-propylpentyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-methylpentyl)amino]-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-(pyridin-2-yl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one;

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-[4-methyl(pyridin-2-yl)]-2,3-dihydro-1H-1,4-benzodiazepin-2-one;

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-[4-trifluoromethyl(pyridin-2-yl)]-2,3-dihydro-1H-1,4-benzodiazepin-2-one;

3-[1-oxo-2-(S)-aminomethyl-heptyl]amino-1-methyl-(5-trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one;

3-[1-oxo-2-(S)-(dimethylamino)methyl-heptyl]amino-1-methyl-5-(trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one; and

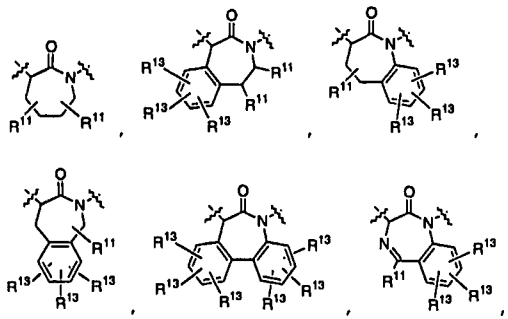
3-(3-isopentyloxy-2-(R)-methyl-1-oxo-propyl)amino-1-methyl-5-(trifluoromethyl)phneyl-2,3-dihydro-1H-1,4-benzodiazepin-2-one.

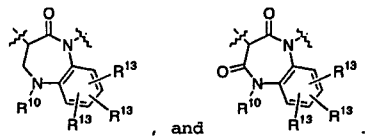
[17] In another preferred embodiment, the present invention provides for a compound, or a pharmaceutically acceptable salt or prodrug thereof, selected from:

(7S)-[(2S)-1-oxo-2-pentyloxy-4-methylpentyl]amino-5-methyl-5H,7H-dibenzo[b,d]azepin-6-one.

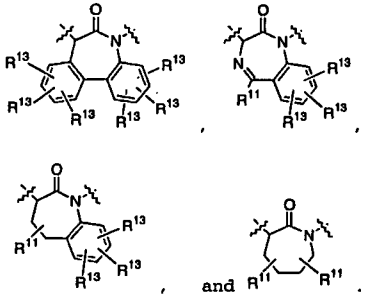
It is appreciated that certain features of the invention, which are, for clarity, described herein in the context of separate embodiments, may also be provided in combination in a single embodiment. As such, it is understood that any and all embodiments of the present invention may be taken in conjunction with any other embodiment to describe additional embodiments of the present invention. Conversely, various features of the invention which are for brevity, described herein in the context of a single embodiment, may also be provided separately or in any subcombination. As such, it is understood that any elements of an embodiment are meant to be combined with any and all other elements from any of the embodiments to describe additional embodiments.

In a preferred embodiment Ring B is selected from:

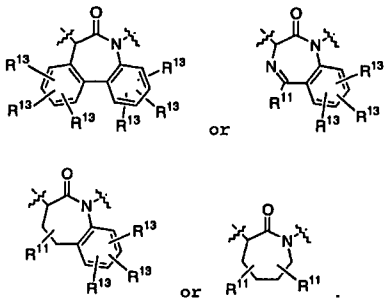




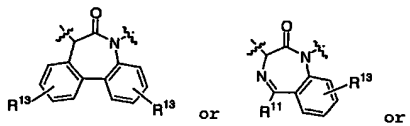
In another preferred embodiment Ring B is selected from:

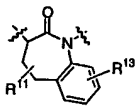


In another preferred embodiment Ring B is singly:



In another preferred embodiment Ring B is singly:


or

or

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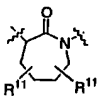

.

Also included in the present invention are compounds as set forth in the embodiments above wherein Q is $-(CR^7R^{7a})_m-R^4$, $-(CR^7R^{7a})_n-S-R^4$, $-(CR^7R^{7a})_n-O-R^4$, or $-(CR^7R^{7a})_m-N(R^{7b})-R^4$.

In a preferred embodiment Q is $-(CHR^7)_m-R^4$, $-(CHR^7)_n-S-R^4$, $-(CHR^7)_n-O-R^4$, or $-(CHR^7)_m-N(R^{7b})-R^4$.

In another preferred embodiment Q is $-(CH_2)_m-R^4$, $-(CH_2)_n-S-R^4$, $-(CH_2)_n-O-R^4$, or $-(CH_2)_m-N(H)-R^4$.

In another preferred embodiment Q is $-(CH_2)_m-R^4$, $-(CH_2)_n-O-R^4$, or $-(CH_2)_m-N(H)-R^4$.

In another preferred embodiment Q is $-CH_2R^4$, $-O-R^4$, $-CH_2OR^4$, or $-CH_2-NH-R^4$.

In another preferred embodiment Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$.

In another preferred embodiment Q is $-CH_2R^4$.
In another preferred embodiment Q is $-CH_2OR^4$ or $-O-R^4$.
In another preferred embodiment Q is $-CH_2OR^4$.
In another preferred embodiment Q is $-O-R^4$.
In another preferred embodiment Q is $-CH_2-NH-R^4$.

In another preferred embodiment Q is $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$,

$-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_2CH_3$, or $-CH_2CH_2CH_2CH_2CH(CH_3)_2$.

In another preferred embodiment Q is $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, or $-CH_2CH_2$-cyclohexyl.

In another preferred embodiment Q is $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$, $-OCH(CH_3)_2$, $-OCH_2CH_2CH_2CH_3$, $-OCH_2CH(CH_3)_2$, $-OCH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH(CH_3)_2$, or $-OCH_2CH_2CH_2CH_2CH(CH_3)_2$.

In another preferred embodiment Q is $-OCH_2$-cyclopropyl, $-OCH_2$-cyclobutyl, $-OCH_2$-cyclopentyl, $-OCH_2$-cyclohexyl, $-OCH_2CH_2$-cyclopropyl, $-OCH_2CH_2$-cyclobutyl, $-OCH_2CH_2$-cyclopentyl, or $-OCH_2CH_2$-cyclohexyl.

In another preferred embodiment Q is $-CH_2OCH_3$, $-CH_2OCH_2CH_3$, $-CH_2OCH_2CH_2CH_3$, $-CH_2OCH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH_2CH_2CH(CH_3)_2$, or $-CH_2OCH_2CH_2CH_2CH_2CH(CH_3)_2$.

In another preferred embodiment Q is $-CH_2OCH_2$-cyclopropyl, CH_2OCH_2-cyclobutyl, CH_2OCH_2-cyclopentyl, CH_2OCH_2-cyclohexyl, $CH_2OCH_2CH_2$-cyclopropyl, $CH_2OCH_2CH_2$-cyclobutyl, $CH_2OCH_2CH_2$-cyclopentyl, or $CH_2OCH_2CH_2$-cyclohexyl.

It is provided that in the definition of Q, when n is 0 then R^4 can not be H.

Also included in the present invention are compounds as set forth in the embodiments above wherein the integer m may be selected from 1, 2, or 3.

In another preferred embodiment the integer m is 1 or 2.
In another preferred embodiment the integer m is 2.
In another preferred embodiment the integer m is 1.

Also included in the present invention are compounds as set forth in the embodiments above wherein the integer n may be selected from 0, 1, or 2; provided that when n is 0 then R^4 can not be H.

In another preferred embodiment the integer n is 0 or 1.
In another preferred embodiment the integer n is 0.
In another preferred embodiment the integer n is 1.
In another preferred embodiment the integer n is 2.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^4 is H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, or C_3-C_{10} carbocycle.

In another preferred embodiment R^4 is C_2-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, or C_3-C_6 cycloaklyl.

In another preferred embodiment R^4 is C_3-C_8 alkyl, C_3-C_8 alkenyl, C_3-C_8 alkynyl, or C_3-C_6 cycloaklyl.

In another preferred embodiment R^4 is C_4-C_8 alkyl, C_4-C_8 alkenyl, C_4-C_8 alkynyl, or C_3-C_6 cycloaklyl.

In another preferred embodiment R^4 is C_2-C_8 alkyl.

In another preferred embodiment R^4 is C_3-C_8 alkyl.

In another preferred embodiment R^4 is C_4-C_8 alkyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^5 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, or (C_3-C_6 cycloalkyl)C_1-C_4 alkyl, ($NR^{15}R^{16}$)C_1-C_4 alkyl.

In another preferred embodiment R^5 is C_2-C_8 alkyl, C_2-C_8 alkenyl, or C_2-C_8 alkynyl.

In another preferred embodiment R^5 is C_3-C_8 alkyl, C_3-C_8 alkenyl, or C_3-C_8 alkynyl.

In another preferred embodiment R^5 is C_4-C_8 alkyl, C_4-C_8 alkenyl, C_4-C_8 alkynyl.

In another preferred embodiment R^5 is C_2-C_8 alkyl.
In another preferred embodiment R^5 is C_3-C_8 alkyl.
In another preferred embodiment R^5 is C_4-C_8 alkyl.
In another preferred embodiment R^5 is (C_3-C_6 cycloalkyl)C_1-C_4 alkyl.
In another preferred embodiment R^5 is ($NR^{15}R^{16}$)C_1-C_4 alkyl.

In another preferred embodiment R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2NH_2$, $-CH_2N(CH_3)_2$, $-CH_2N(CH_2CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, or $-CH_2$-cyclohexyl.

In another preferred embodiment R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, or $-CH_2CH_2CH_2CH_2CH(CH_3)_2$.

In another preferred embodiment R^5 is $-CH_2NH_2$, $-CH_2N(CH_3)_2$, $-CH_2N(CH_2CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2N(CH_3)_2$, or $-CH_2CH_2N(CH_2CH_3)_2$.

In another preferred embodiment R^5 is $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, or $-CH_2$-cyclohexyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^6 is H.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^{11} is
H, $NR^{18}R^{19}$;
C_1-C_4 alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 cycloalkyl substituted with 0-3 R^{11b}; or
pyridinyl substituted with 0-3 R^{11b};

wherein R^{11a} is phenyl substituted with 0-3 R^{11b};
wherein R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, and propoxy.

In another preferred embodiment R^{11} is independently selected from
H, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-,
3-F-phenyl, (3-F-phenyl)CH_2-, (3-F-phenyl)CH_2CH_2-,
2-F-phenyl, (2-F-phenyl)CH_2-, (2-F-phenyl)CH_2CH_2-,
4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-,
3-Cl-phenyl, (3-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2CH_2-,
4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-,
3-CH_3-phenyl, (3-CH_3-phenyl)CH_2-, (3-CH_3-phenyl)CH_2CH_2-,
4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, (4-CF_3-phenyl)CH_2CH_2-,
pyrid-2-yl, 4-F-pyrid-2-yl, 4-Cl-pyrid-2-yl,
4-CH_3-pyrid-2-yl, 4-CF_3-pyrid-2-yl, pyrid-3-yl,
4-F-pyrid-3-yl, 4-Cl-pyrid-3-yl, 4-CH_3-pyrid-3-yl,
4-CF_3-pyrid-3-yl, and pyrid-4-yl.

In another preferred embodiment R^{11} is independently selected from
H, methyl, ethyl, phenyl, 4-F-phenyl, 3-F-phenyl,
2-F-phenyl, 4-Cl-phenyl, 3-Cl-phenyl, 4-CH_3-phenyl,

3-CH_3-phenyl, 4-CF_3-phenyl, pyrid-2-yl, 4-F-pyrid-2-yl,
4-Cl-pyrid-2-yl, 4-CH_3-pyrid-2-yl, and 4-CF_3-pyrid-2-yl.

Also included in the present invention are compounds as set forth in the embodiments above wherein W may be selected from a bond, -CH_2-, -CH_2CH_2-, or -$CH(CH_3)$-.

In another preferred embodiment W is a bond or -$(CH_2)_p$-.
In another preferred embodiment W is a bond, -CH_2-, or -CH_2CH_2-.
In another preferred embodiment W is a bond or -CH_2-.
In another preferred embodiment W is -CH_2-.
In another preferred embodiment W is a bond.

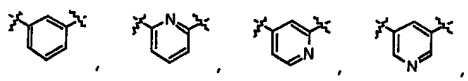
Also included in the present invention are compounds as set forth in the embodiments above wherein the integer p may be selected from 0, 1, 2, or 3.

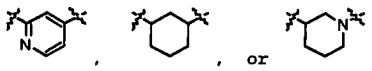
In another preferred embodiment the integer p is 0, 1 or 2.
In another preferred embodiment the integer p is 0 or 1.
In another preferred embodiment the integer p is 0.

Also included in the present invention are compounds as set forth in the embodiments above wherein X is a bond, C_6-C_{10} aryl, C_3-C_{10} carbocycle or 5 to 10 membered heterocycle.

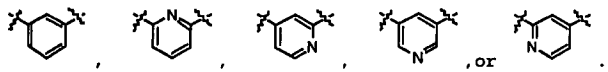
In another preferred embodiment X is a bond, phenyl, C_3-C_6 carbocycle, or 5 to 6 membered heterocycle.
In another preferred embodiment X is a bond, phenyl, C_3-C_6 cycoalkyl, or 5 to 6 membered heterocycle.

In another preferred embodiment X is a bond;





In another preferred embodiment X is a bond;



In another preferred embodiment X is a bond or phen-1,3-diyl.

In another preferred embodiment X is phen-1,3-diyl.

In another preferred embodiment X is a bond.

Also included in the present invention are compounds as set forth in the embodiments above wherein Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, $-C(=O)O-$, or $-OC(=O)-$.

In another preferred embodiment Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, $-C(=O)NH-$, $-NHC(=O)-$, $-NHS(=O)_2-$, $-S(=O)_2NH-$, $-NHS(=O)-$, $-S(=O)NH-$, $-C(=O)O-$, or $-OC(=O)-$.

In another preferred embodiment Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, or $-N(CH_2CH_3)-$.

In another preferred embodiment Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, or $-N(CH_3)-$.

In another preferred embodiment Y is a bond, $-C(=O)-$, $-O-$, $-NH-$, or $-N(CH_3)-$.

In another preferred embodiment Y is $-O-$.

In another preferred embodiment Y is $-NH-$.

In another preferred embodiment Y is $-N(CH_3)-$.

In another preferred embodiment Y is a bond.

Also included in the present invention are compounds as set forth in the embodiments above wherein Z is

C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl,
C_1-C_2 alkyl substituted with 1-2 R^{12a};
phenyl substituted with 0-4 R^{12b};
C_3-C_6 carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b};
wherein R^{12a} is phenyl substituted with 0-4 R^{12b};
C_3-C_6 carbocycle substituted with 0-4 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; and
wherein R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, and $-OCF_3$;

In another preferred embodiment Z is
C_1-C_2 alkyl substituted with 1-2 R^{12a}; or
phenyl substituted with 0-4 R^{12b};
wherein R^{12a} is phenyl substituted with 0-4 R^{12b};
wherein R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, and $-OCF_3$;

In another preferred embodiment Z is C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_2-C_4 alkynyl.

In another preferred embodiment Z is phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl, 2-Cl-phenyl, 3-Cl-phenyl,

4-Cl-phenyl, 2,3-diF-phenyl, 2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl, 3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl, 2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl, 3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl, 3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl, 3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl, 4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl, 2-CF_3O-phenyl, 3-CF_3O-phenyl, 4-CF_3O-phenyl, furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl, 4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl, 1-benzimidazolyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, N-piperinyl, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-, (3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, (2-MeO-phenyl)CH_2-, (3-MeO-phenyl)CH_2-, (4-MeO-phenyl)CH_2-, (2-Me-phenyl)CH_2-, (3-Me-phenyl)CH_2-, (4-Me-phenyl)CH_2-, (2-MeS-phenyl)CH_2-, (3-MeS-phenyl)CH_2-, 4-MeS-phenyl)CH_2-, (2-CF_3O-phenyl)CH_2-, (3-CF_3O-phenyl)CH_2-, (4-CF_3O-phenyl)CH_2-, (furanyl)CH_2-, (thienyl)CH_2-, (pyridyl)CH_2-, (2-Me-pyridyl)CH_2-, (3-Me-pyridyl)CH_2-, (4-Me-pyridyl)CH_2-, (1-imidazolyl)CH_2-, (oxazolyl)CH_2-, (isoxazolyl)CH_2-, (1-benzimidazolyl)CH_2-, (cyclopropyl)CH_2-, (cyclobutyl)CH_2-, (cyclopentyl)CH_2-, (cyclohexyl)CH_2-, (morpholino)CH_2-, (N-pipridinyl)CH_2-, or (phenyl)$_2$CH-.

In another preferred embodiment Z is phenyl, 2-F-phenyl,

3-F-phenyl, 4-F-phenyl, 2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl, 2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl, 3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl, 2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl, 3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl, 3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl, 3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl, 4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl, 2-CF_3O-phenyl, 3-CF_3O-phenyl, 4-CF_3O-phenyl, or 4-phenyl-phenyl.

In another preferred embodiment Z is phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-, (3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, (2-MeO-phenyl)CH_2-, (3-MeO-phenyl)CH_2-, (4-MeO-phenyl)CH_2-, (2-Me-phenyl)CH_2-, (3-Me-phenyl)CH_2-, (4-Me-phenyl)CH_2-, (2-MeS-phenyl)CH_2-, (3-MeS-phenyl)CH_2-, 4-MeS-phenyl)CH_2-, (2-CF_3O-phenyl)CH_2-, (3-CF_3O-phenyl)CH_2-, (4-CF_3O-phenyl)CH_2-, or (phenyl)$_2$CH-.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^{13}, at each occurrence, is independently selected from H, F, Cl, OH, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, and $-CF_3$.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^{14} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

Also included in the present invention are compounds as set forth in the embodiments above wherein R^{15}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, and phenethyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein in the moiety R^4-(CR^7R^{7a})m-(R^5)CH- of Formula (I) when R^4 is an alkyl, alkenyl, or alkynyl moiety; and R^5 is an alkyl, alkenyl, or alkynyl moiety; then the total number of carbon atoms in the backbone of R^4-(CR^7R^{7a})m-(R^5)CH- equals nine or more. For example, when R^5 is methyl, then R^4-(CR^7R^{7a})m- is heptyl (branched or linear) or greater. For example, when R^5 is ethyl, then R^4-(CR^7R^{7a})m- is hexyl (branched or linear) or greater. It is understood that the proviso is only intended to define the number of carbon atoms, continuously linked in the backbone of the R^4-(CR^7R^{7a})m-

(R^5)CH- moiety and not meant to limit substitution by R^{4a} or R^{5b} on the R^4-(CR^7R^{7a})m-(R^5)CH-.

Also included in the present invention are compounds as set forth in the embodiments above wherein in the moiety R^4-O(CR^7R^{7a})n-(R^5)CH- of Formula (I) when -(CR^7R^{7a})n-(R^5)CH- is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_3-C_{10} cycloalkyl-C_1-C_4 alkyl, C_6-C_{10} aryl-C_1-C_4 alkyl, C_6-C_{10} aryl-C_2-C_4 alkynyl, then R^4 is other than H, methyl, ethyl, isopropyl, phenyl, or benzyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein in the moiety R^4-O(CR^7R^{7a})n-(R^5)CH- of Formula (I) when -(CR^7R^{7a})n-(R^5)CH- is C_1-C_4 alkyl, then R^4 is other than C_1-C_4 alkyl.

Also included in the present invention are compounds as set forth in the embodiments above wherein in the moiety R^4-$NR^{7b}(CR^7R^{7a})$n-(R^5)CH- of Formula (I) when -(CR^7R^{7a})n-(R^5)CH- is C_2-C_4 alkyl, then R^4 is other than C_2-C_4 alkyl.

In a second embodiment, the present invention provides a pharmaceutical composition comprising a compound of Formula (I) and a pharmaceutically acceptable carrier.

In a third embodiment, the present invention provides a method for the treatment of neurological disorders associated with β-amyloid production comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Formula (I).

In a preferred embodiment the neurological disorder associated with β-amyloid production is Alzheimer's Disease.

In a fourth embodiment, the present invention provides a method for inhibiting γ-secretase activity for the treatment of a physiological disorder associated with inhibiting γ-secretase activity comprising administering to

a host in need of such inhibition a therapeutically effective amount of a compound of Formula (I) that inhibits γ-secretase activity.

Thus, the present invention provides a method for inhibiting γ-secretase activity comprising administering to a host in need of such inhibition a therapeutically effective amount of a compound of Formula (I) that inhibits γ-secretase activity.

In a preferred embodiment the physiological disorder associated with inhibiting γ-secretase activity is Alzheimer's Disease.

In a fifth embodiment, the present invention provides a compound of Formula (I) for use in therapy.

In a preferred embodiment the present invention provides a compound of Formula (I) for use in therapy of Alzheimer's Disease.

In a sixth embodiment, the present invention provides for the use of a compound of Formula (I) for the manufacture of a medicament for the treatment of Alzheimer's Disease.

DEFINITIONS

As used herein, the term "Aβ" denotes the protein designated Aβ, β-amyloid peptide, and sometimes β/A4, in the art. Aβ is an approximately 4.2 kilodalton (kD) protein of about 39 to 43 amino acids found in amyloid plaques, the walls of meningeal and parenchymal arterioles, small arteries, capillaries, and sometimes, venules. The isolation and sequence data for the first 28 amino acids are described in U.S. Pat. No 4,666,829. The 43 amino acid sequence is:

1									
Asp	Ala	Glu	Phe	Arg	His	Asp	Ser	Gly	Tyr
11									
Glu	Val	His	His	Gln	Lys	Leu	Val	Phe	Phe
21									
Ala	Glu	Asp	Val	Gly	Ser	Asn	Lys	Gly	Ala

31									
Ile	Ile	Gly	Leu	Met	Val	Gly	Gly	Val	Val
41									
Ile	Ala	Thr							

The term "APP", as used herein, refers to the protein known in the art as β amyloid precursor protein. This protein is the precursor for Aβ and through the activity of "secretase" enzymes, as used herein, it is processed into Aβ. Differing secretase enzymes, known in the art, have been designated β secretase, generating the N-terminus of Aβ, α secretase cleaving around the 16/17 peptide bond in Aβ, and "γ secretases", as used herein, generating C-terminal Aβ fragments ending at position 38, 39, 40, 42, and 43 or generating C-terminal extended precursors which are subsequently truncated to the above polypeptides.

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a

substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced.

When any variable (e.g., R^{5b}) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-3 R^{5b}, then said group may optionally be substituted with up to three R^{5b} groups and R^{5b} at each occurrence is selected independently from the definition of R^{5b}. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein, "alkyl" or "alkylene" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms; for example, "C_1-C_6 alkyl" denotes alkyl having 1, 2, 3, 4, 5, or 6 carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, pentyl, and hexyl. Preferred "alkyl" group, unless otherwise specified, is "C_1-C_4 alkyl". Additionally, unless otherwise specified, "propyl" denotes n-propyl or i-propyl; "butyl" denotes n-butyl, i-butyl, sec-butyl, or t-butyl.

As used herein, "alkenyl" or "alkenylene" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more unsaturated carbon-carbon bonds which may occur in any stable point

along the chain. Examples of "C_2-C_6 alkenyl" include, but are not limited to, ethenyl, 1-propenyl, 2-propenyl, 1-butenyl, 2-butenyl, 3-butenyl, 3-methyl-2-butenyl, 2-pentenyl, 3-pentenyl, hexenyl, and the like.

As used herein, "alkynyl" or "alkynylene" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more carbon-carbon triple bonds which may occur in any stable point along the chain, such as ethynyl, 1-propynyl, 2-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, and the like.

"Alkoxy" or "alkyloxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. Preferred alkoxy groups are methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy. Similarly, "alkylthio" or "thioalkoxy" is represents an alkyl group as defined above with the indicated number of carbon atoms attached through a sulphur bridge.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo. Unless otherwise specified, preferred halo is fluoro and chloro. "Counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, sulfate, and the like.

"Haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example $-C_vF_w$ where v = 1 to 3 and w = 1 to (2v+1)). Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, pentachloroethyl, 2,2,2-trifluoroethyl, 2,2-difluoroethyl, heptafluoropropyl, and heptachloropropyl. "Haloalkoxy" is intended to mean a haloalkyl group as defined above with the indicated number

of carbon atoms attached through an oxygen bridge; for example trifluoromethoxy, pentafluoroethoxy, 2,2,2-trifluoroethoxy, and the like. "Halothioalkoxy" is intended to mean a haloalkyl group as defined above with the indicated number of carbon atoms attached through a sulphur bridge.

"Cycloalkyl" is intended to include saturated ring groups, having the specified number of carbon atoms. For example, "C_3-C_6 cycloalkyl" denotes such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

As used herein, "carbocycle" is intended to mean any stable 3- to 7-membered monocyclic or bicyclic or 7- to 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane (decalin), [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, or tetrahydronaphthyl (tetralin). Preferred "carbocycle" are cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

As used herein, the term "heterocycle" or "heterocyclic ring" is intended to mean a stable 5- to 7-membered monocyclic or bicyclic or 7- to 14-membered bicyclic heterocyclic ring which is saturated partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and 1, 2, 3 or 4 heteroatoms independently selected from the group consisting of N, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom which results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. If

specifically noted, a nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. It is preferred that the total number of S and O atoms in the heterocycle is not more than 1.

Examples of heterocycles include, but are not limited to, 1H-indazole, 2-pyrrolidonyl, 2H,6H-1,5,2-dithiazinyl, 2H-pyrrolyl, 3H-indolyl, 4-piperidonyl, 4aH-carbazole, 4H-quinolizinyl, 6H-1,2,5-thiadiazinyl, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazalonyl, carbazolyl, 4a*H*-carbazolyl, b-carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinylperimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, piperidonyl, 4-piperidonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl,

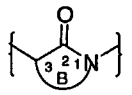
thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, xanthenyl. Preferred 5 to 10 membered heterocycles include, but are not limited to, pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl. Preferred 5 to 6 membered heterocycles include, but are not limited to, pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl; more preferred 5 to 6 membered heterocycles include, but are not limited to, pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, and tetrazolyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

As used herein, the term "aryl", "C_6-C_{10} aryl" or aromatic residue, is intended to mean an aromatic moiety containing the specified number of carbon atoms; for example phenyl, pyridinyl or naphthyl. Preferred "aryl" is phenyl. Unless otherwise specified, "aryl" may be unsubstituted or substituted with 0 to 3 groups selected from H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, amino, hydroxy, Cl, F, Br, I, CF_3, SCH_3, $S(O)CH_3$, SO_2CH_3, $-N(CH_3)_2$, $N(CH_3)H$, CN, NO_2, OCF_3, $C(=O)CH_3$, CO_2H, CO_2CH_3, or C_1-C_4 haloalkyl.

As used herein, the term "heteroaryl fused radical" is intended to denote a 5 or 6 membered aromatic ring comprising carbon atoms and one or two heteroatoms selected from nitrogen, sulphur and oxygen. The 5 or 6 membered ring is fused to two adjacent atoms of a second ring, i.e. forming a bicyclic ring system, wherein the second ring is lactam ring B. Examples of a "heteroaryl fused radical"

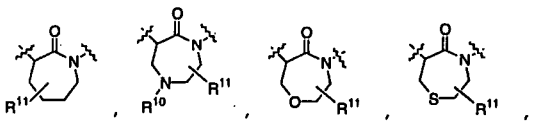
are furanyl, imidazolyl, isoxazolyl, oxazolyl, pyrrolyl, thiophenyl, thiazolyl, isothiozalyl, pyridyl, pyridazinyl, pyrimidinyl, and pyrazinyl.

The phrase "additional lactam carbons", as used herein, is intended to denote the number of optional carbon atoms in the lactam ring B of Formula (I). Formula (I"):

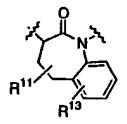


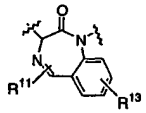
(I")

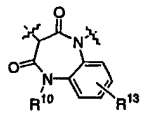
represents the lactam ring B of Formula (I). Additional lactam carbons are carbons in lactam ring B other than the carbons numbered 2 and 3 in the backbone of the formula. The additional lactam carbons may be optionally replaced by a heteroatom selected from oxygen, nitrogen and sulfur. Lactam ring B contains 1, 2, 3, 4, 5, 6 or 7 optional carbons, wherein one optional carbon may optionally be replaced by a heteroatom, such that the total number of members of lactam ring B, including atoms numbered 1, 2 and 3 in the backbone, does not exceed 10. It is preferred that the total number of atoms of lactam ring B is 6, 7 or 8; it is more preferred that the total number of atoms of lactam ring B is seven. It is further understood that lactam ring B may optionally be unsaturated or partially unsaturated (i.e. two adjacent atoms in the ring form a double bond) wherein the backbone of lactam ring B may contain one, two or three double bonds. Examples of lactam ring B include:

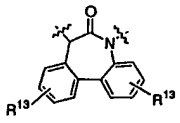


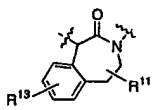
B1 B2 B3 B4

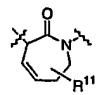

B5

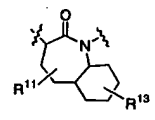

B6

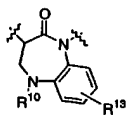

B8

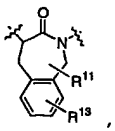

B9

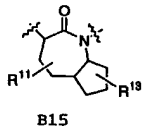

B10

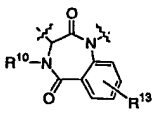

B11


B12


B13


B14

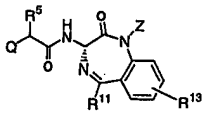

B15


B16

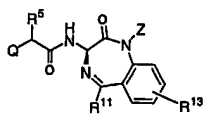
but are not intended to limit the invention. Preferred examples of lactam ring B are B1, B2, B5, B6, B8, B9, B13, and B16; more preferred examples of lactam ring B are B1, B6, B8, B9, and B13. Preferred examples of substituent R^{10} or R^{11} on lactam B are hydrogen, methyl, ethyl, phenyl, benzyl, phenethyl, 4-fluorophenyl, 4-chlorophenyl, 4-methylphenyl, 4-CF_3-phenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-methylphenyl)methyl, (4-CF_3-phenyl)methyl, (4-fluorophenyl)ethyl, (4-chlorophenyl)ethyl, (4-methylphenyl)ethyl, (4-CF_3-

phenyl)ethyl, and 2-, 3-, and 4-pyridinyl. More preferred examples of substituent R^{10} or R^{11} on lactam B are methyl, ethyl, phenyl, 4-fluorophenyl, 4-chlorophenyl, 4-CF_3-phenyl, (4-fluorophenyl)methyl, (4-chlorophenyl)methyl, (4-CF_3-phenyl)methyl, and 2-, 3-, and 4-pyridinyl. Preferred examples of R^{13} on lactam B are F, Cl, OH, methyl, ethyl, methoxy, and trifluoromethyl.

The compounds herein described may have asymmetric centers. One enantiomer of a compound of Formula (I) may display superior biological activity over the opposite enantiomer. For example carbon 3 of lactam ring B Formula (I") may exist in either an S or R configuration. Thus, an R or S configuration at carbon 3 in Formula (I"-3R) and (I"-3S) are considered part of the invention. Examples of such configuration include,


(I"-3S)

and


(I"-3R)

but are not intended to be limited to this example of ring B. When required, separation of the racemic material can be achieved by methods known in the art. Additionally when the carbon atom to which Q and R^5 are attached is chiral, both the R and S configurations of the carbon atom are considered part of the invention.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

"Prodrugs" are intended to include any covalently bonded carriers which release the active parent drug according to formula (I) *in vivo* when such prodrug is

administered to a mammalian subject. Prodrugs of a compound of formula (I) are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of formula (I) wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug or compound of formula (I) is administered to a mammalian subject, cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and acetamide, formamide, and benzamide derivatives of amine functional groups in the compounds of formula (I), and the like.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

SYNTHESIS

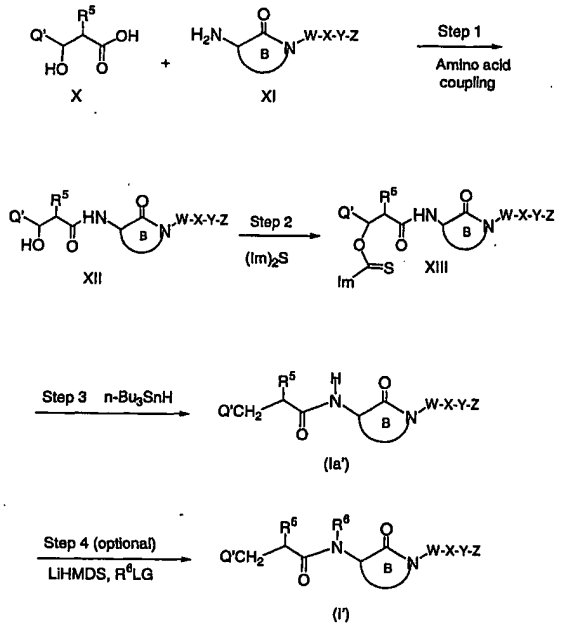
The compounds of the present invention can be prepared in a number of ways well known to one skilled in the art of organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those described below. All references cited herein are hereby incorporated in their entirety herein by reference.

The novel compounds of this invention may be prepared using the reactions and techniques described in this section. The reactions are performed in solvents appropriate to the reagents and materials employed and are suitable for the transformations being effected. Also, in the description of the synthetic methods described below, it is to be understood that all proposed reaction

conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment and workup procedures, are chosen to be the conditions standard for that reaction, which should be readily recognized by one skilled in the art. It is understood by one skilled in the art of organic synthesis that the functionality present on various portions of the molecule must be compatible with the reagents and reactions proposed. Such restrictions to the substituents which are compatible with the reaction conditions will be readily apparent to one skilled in the art and alternate methods must then be used.

Compounds of Formula (I) of the present invention can be synthesized by the method of Scheme 1 comprising : step 1, an amino acid coupling; followed by step 2, a radical reduction; and an optional step 3, a reaction with R^6-LG where LG is a leaving group, for example halide, mesylate, triflate or other leaving group well known to one skilled in the art. See Scheme 1. In the method of Scheme 1, step 1, a W-X-Y-Z-substituted aminolactam, XI, is coupled with an β-hydroxy acid X to form a lactam XII. The amine XI is coupled to an appropriately substituted carboxylic acid or acid chloride by methods well described in the literature for making amide bonds, for example, TBTU in DMF with a base, for example, NMM to give the elaborated compound XII. In step 2, the lactam XII is then reacted with thiocarbonyl diimidazole to form a carbonyl derivative XIII which is then converted to a compound of Formula (Ia') by a radical hydride reduction. The deoxygenation of lactam XII to a

Scheme 1

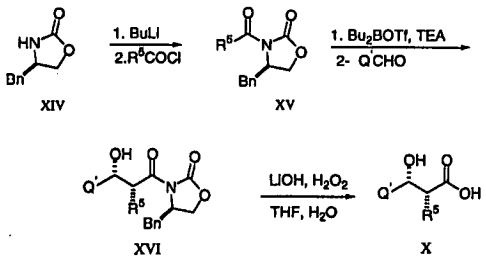


compound of Formula (Ia') can be prepared by means of a free radical deoxygenation procedure [Barton and McCarobie, J. Chem. Soc. Perkin Trans. 1, 1574 (1975); Robins et al., J. Am Chem. Soc. 103, 933 (1981); 105, 4059 (1983); Barton and Motherwell, Pure & Appl. Chem., 53, 15 (1981)]. This process entails the conversion of the free hydroxy group in compound XII to a suitable derivative, for example, a thiono-ester XIII. Upon treatment with a hydrogen radical source in the presence of a radical initiator, compound XIII undergoes reductive deoxygenation to furnish compounds of general structure (Ia'). For such deoxygenation reactions, suitable sources of hydrogen radicals are the trialkyltin hydrides (e.g. tributyltin hydride) or tris

(trialkylsilyl) silanes (e.g. $(Me_3Si)_3SiH$) [Schummer and Hofle, Syn. Lett. 106 (1990); Ballestri et al., J. Org. Chem. 56, 678 (1991)], and suitable radical initiators are provided by azaisobutyronitrile (AIBN), heat, or irradiation. A compound of Formula (Ia') can be alkylated using standard bases, for example LDA, NaH, or NaHMDS, to deprotonate the amide followed by addition of an alkylating agent with an appropriate leaving group (LG) for example halide, mesylate, or triflate, in an appropriate solvent to provide a compound of Formula (I') with an R^6 substituent.

Aldol derivatives X (Scheme 2) can be prepared by the procedure of Evans (D. A. Evans et al, *Org. Synth.* **1990**, *68*, 83-90). Acylation of an oxazolidinone XIV with an acid chloride provides acylated oxazolidinone XV. The reaction of XV with an aldehyde Q'CHO in the presence of dibutyl boron triflate gives an aldol product XVI. The chiral auxiliary of the aldol product XVI is then removed to give a β-hydroxy-carboxylic acid product X. Additional examples are found in D. A. Evans *Aldrichimica Acta* **1982**, *15*, 23-32. Alternative syntheses of compound X can be accomplished by the methods of Crimmins (M. T. Crimmins et al, *J. Am. Chem. Soc.* **1997**, *119*, 7883-7884), Paterson (I. Paterson et al, *Org. React.* **1997**, *51*, 1-200) and Mukaiyama (T. Mukaiyama et al, Org. React. 1994, 1-104).

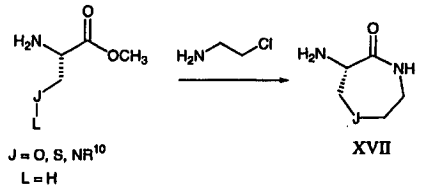
Scheme 2



Methods for the synthesis of lactams useful as intermediates in the synthesis of compounds as contemplated by the present invention in lactam ring B in Formula (I), including amino benzodiazepinones, amino dibenzoazepinones and other related heterocycles, are known in the art and are disclosed in a number of references including PCT publication number WO98/28268, WO99/66934, and WO00/07995, which are hereby incorporated by reference. Additional references include Bock, et al, J. Org. Chem., 1987, *52*, 3232-3239; Sherrill et al, J. Org. Chem., 1995, *60*, 730-734; and Walsh, D. A., Synthesis, September 1980, p.677; and Brown, at. al., Tetrahedron Letters, 1971, 8, 667-670.

An example of an L-α-amino-β-thio-ε-caprolactam, as shown in Scheme 3, where ring B is the amino lactam of XVII and J is a sulfur atom has been reported in the literature. See S. A. Ahmed et al, FEBS Letters, (1984), vol. 174, pages 76-9. One skilled in the art can extend this methodology to the synthesis of β-amino and oxygen containing rings by analogy. The sulfur-containing molecules can also be oxidized to the sulfoxide and sulfone by methods known to one skilled in the art.

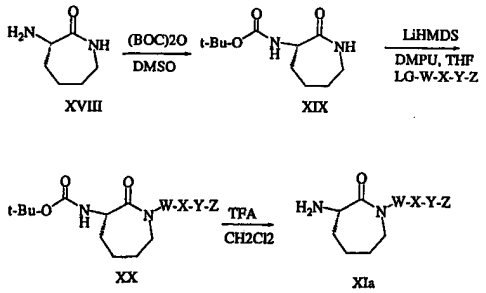
Scheme 3



The WXYZ-substituted amino lactam XI can be formed by alkylation of an amino lactam with WXYZ-LG. For example in Scheme 4, the α-amine of compound XVIII can be protected with a BOC group. The protected α-amine XVIII of the α-amino-ε-caprolactam can be prepared by methods well known in the literature for amino protecting groups as discussed

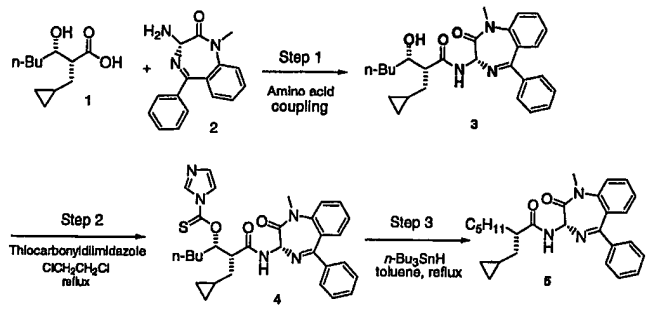
in Theodora W. Greene's book "Protective Groups in Organic Synthesis", like *N*-Boc using di-*t*-butyldicarbonate in an appropriate solvent like DMSO. The lactam nitrogen of compound XV can be alkylated by generating the anion with bases such as LDA, lithium bis(trimethylsilyl)amide or sodium hydride in solvents like THF, with or without cosolvents such as DMPU or HMPA and reacting this with a variety of groups containing leaving groups (LG) like bromide, iodide, mesylate or tosylate. Alkylating agents such as α-bromo amides, ketones and acids can be prepared by a number of literature methods including halogenation of amino acids by diazotization or are commercially available. Other suitable alkylating agents such as alkyl, allylic and benzylic halides can be formed form a variety of precursors such as free-radical addition of halides or activation of alcohols, and other chemistries known to those skilled in the art. For discussion of these types of reactions, see Carey, F.A. and Sundberg, R. J., Advanced Organic Chemistry, Part A, *New York*: Plenum Press, 1990, pages 304-305, 342-347, 695-698. The *N*-Boc protecting group can be removed by any number of methods well known in the literature like TFA in methylene chloride to give the compound XIa.

Scheme 4



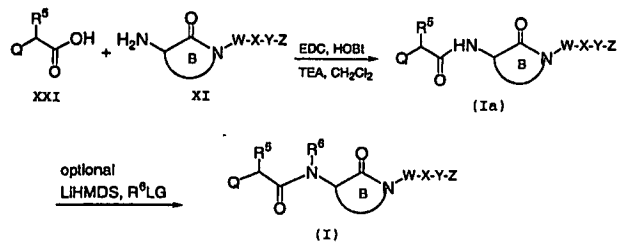
An example of the method of Scheme 1 is illustrated in the preparation of compound **5** (Scheme 5). The aldol product **3** is obtained from an amino acid coupling of an β-hydroxyacid **1** and a benzodiazepine **2** using a standard coupling procedure. The coupled aldol product **3** is reacted with thiocarbonyl diimidazole in 1,2-dichloroethane to form a thiocarbamate **4**. Reduction of thiocarbamate **4** with tri-*n*-butyltin hydride provides a benzodiazepine **5**.

Scheme 5



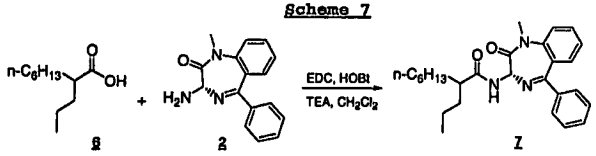
Alternatively, compounds of Formula (I) can be prepared according to Scheme 6. An acid XXI is coupled with a W-X-Y-Z-substituted aminolactam, XI, to give a compound of Formula (Ia) using methods commonly used in peptide syntheses, such as DCC, EDC, CDI, BOP, PyBOP, HATU, HBTU and phenyl ester mediated coupling, as described in A. R. Chamberlin, *Chem. Rev.* **1997**, *97*, 2243-2266. Subsequently, the amide nitrogen of compound (Ia) can optionally react with an R^6-LG to give a compound of Formula (I).

Scheme 6



An example of the method of Scheme 6 is illustrated in the preparation of compound 7 (Scheme 7). Carboxylic acid of formula 6 (commercially available) is coupled with 3-amino-1,4-benzodiazepin-2-one 2 (Sherrill and Sugg, J. Org. Chem. 1995, 60, 730-734; Bock et al., J. Med. Chem., 1993, 36, 4276-4292) in the presence of EDC and HOBt to give compound 7 (S. Nozaki et al, *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2165-2168). General methods for preparing compounds similar to compound 6 can be found in Evans, D. A., et al., *J. Am. Chem. Soc.* **1990**, *112*, 5290, Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23, and Ponpipom, M. M., Hagmann, W. K. *Tetrahedron* **1999**, *55*, 6749.

Scheme 7

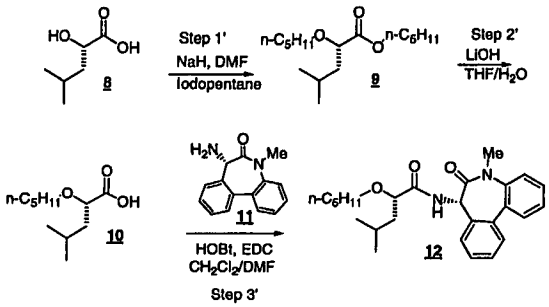


Another example of the method of Scheme 6 is illustrated in the preparation of compound 12 (Scheme 8). In step 3', a chiral lactic acid derivative 10 is coupled with 7-amino-6,7-dihydro-5-methyl-6-oxo-5H-dibenz[b,d]azepin 11 in the presence of HOBt and EDC to afford compound 12.

Compound 11 can be prepared by the methods describe in PCT patent application WO 99/32453. The chiral lactic acid

derivative 10 is prepared from bis-alkylation of (2S)-2-hydroxy-4-methylpentanoic acid 8 with iodopentane to give the lactate 9 in step 1'. Subsequent hydrolysis of lactate 9 using LiOH in THF/H_2O affords the chiral lactic acid derivative 10 in step 2'. Alternatively, compound 10 and other similar chiral lactic acid derivatives can be prepared by the methods described in J.Org. Chem., **1986**,*51*, 2402, and Chem.Rev., **1992**,*92*, 919.

Scheme 8



Examples

Chemical abbreviations used in the Examples are defined as follows: "DMPU" for 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidone, "TBTU" for O-(1H-benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate, "BOP" for benzotriazol-1-yloxytris-(dimethylamino)-phosphonium hexafluorophosphate, "NMM" for N-methylmorpholine, "EDC" for 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochlordie, "HOBt" for 1-hydroxybenzotriazole hydrate, "TEA" for triethyl amine, "LiHMDS" for lithium bis(trimethylsilyl)amide, "HMPA" for hexamethylphosphoramide, "LDA" for lithium diisopropylamide, "DCC" for 1,3-dicyclohexylcarbodiimide, "PyBoP" for benzotriazole-1-yl-oxy-tris-pyrrolidino-

phosphonium hexafluorophosphate, and "HATU" for O-(7-azabenzotriazol-1-yl)-N, N, N', N'-tetramethyluronium hexafluorophosphate. "HPLC" is an abbreviation used herein for high pressure liquid chromatography.

Compounds of the present invention are generally purified by HPLC using conditions known to one skilled in the art. If necessary, organic layers can be dried over sodium sulfate unless otherwise indicated. However, unless otherwise indicated, the following conditions are generally applicable.

HPLC Condition A:

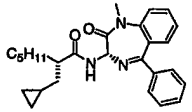
Reverse-phase HPLC can be carried out using a Vydac C-18 column with gradient elution from 10% to 100 % buffer B in buffer A (buffer A: water containing 0.1% trifluoroacetic acid, buffer B: 10% water, 90% acetonitrile containing 0.1% trifluoroacetic acid).

HPLC Condition B:

Alternatively, reverse-phase HPLC can be carried out using a Vydac C-18 column with gradient elution from 10% to 90 % acetonitrile in water.

Example 1

(3S)-3-[(1-oxo-(2S)-2-cyclopropylmethyl-heptyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one



Step 1: Preparation of compound 3(S)-[(1-oxo-(2R)-2-cyclopropylmethyl-(3S)-3-hydroxy-heptyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one, 3. Compound 2 (Scheme 5) was prepared according to the method described in 1) Sherrill and Sugg, J. Org. Chem. 1995, 60, 730-734; 2) Bock et al., J. Med. Chem., 1993, 36, 4276-4292; and 3) Paul J. Reider et al J. Org. Chem. 1987, 52, 955. Compound 1 was prepared by the procedure of Evans D.A. Evans et al, *Org. Synth.* **1990**, *68*, 83-90 (See Scheme 2, Q' is n-Bu and R^5 is cyclopropylmethyl). A mixture of acid 1 (100 mg, 0.500 mmol) and a camphorsulphonate salt of compound 2 (249 mg, 0.500 mmol) in 2 mL of methylene chloride was stirred at 0 °C. 1-Hydroxybenzotriazole hydrate (81 mg, 0.60 mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (192 mg, 1.00 mmol) and triethylamine (0.29 mL, 2.1 mmol) were added sequentially. After the mixture was stirred for 16 h, 30 mL of ethyl acetate was added. The organic layer was washed with 5% $NaHCO_3$ (30 mL) and brine (30 mL), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Purification by flash column chromatography (50% ethyl acetate – hexane) afforded 130 mg (58%) of product 3; MS (ESI): 448 (M+H), 470 (M+Na), 446 (M-H).

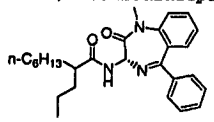
Step 2: Preparation of 3(S)-[((2R)-2-cyclopropylmethyl-(3S)-3-((1-imidazolylthionyl)oxy)-1-oxoheptyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one, 4. Compound 3 (224 mg, 0.500 mmol), from step 1, and 1,1'-(thiocarbonyl)-diimidazole (178 mg, 1.00 mmol) were refluxed in 5 mL of 1,2-dichloroethane under nitrogen for 30 h (Scheme 5). An additional portion of 1,1'-(thiocarbonyl)diimidazole (180 mg, 1.00 mmol) was added, and reflux was continued for an additional 30 h. 20 mL of ethyl acetate was added. The organic layer was washed with water (30 mL) and brine (30 mL), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Purification by flash chromatography (60% ethyl acetate-hexane) afforded 198 mg (71%) of 4 as a colorless gel. ^1H NMR (300 MHz, $CDCl_3$) δ 8.56 (1 H, br s), 7.82 (1 H, br s), 7.24 - 7.64 (10 H, m), 7.04 (1 H, br s), 5.96 (1 H, m), 5.54 (1 H, d, J = 7.7 Hz), 3.47 (3 H, s), 2.97 (1 H, m), 1.86 - 1.06 (3 H, m), 1.24 - 1.45 (5 H, m), 0.94 (3 H, t,

J = 6.6 Hz), 0.81 (1 H, m), 0.50 (2 H, m), 0.13 (1 H, m), 0.06 (1 H, m); MS (APCI): 558 (M+H), 592 (M+Cl).

Step 3: Preparation of (3S)-3-[(1-oxo-(2R)-2-cyclopropylmethyl-heptyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one, **5**. A solution of **4** (190 mg, 0.350 mmol), from step 2, in 10 mL of dry and degassed toluene was heated to reflux. A solution of tri-*n*-butyltin hydride (210 mg, 0.700 mmol) in 1 mL of toluene was added dropwise over 30 min. After an additional 5 h of reflux, the reaction was cooled, concentrated under reduced pressure. The crude mixture was purified by flash chromatography (elution with hexanes initially to remove tin-containing materials, then with 40% ethyl acetate-hexane) to afford 128 mg (85%) of compound **5** as a colorless gel. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 - 7.66 (10 H, m), 5.60 (1 H, d, J = 8.4 Hz), 3.47 (3 H, s), 2.30 (1 H, m), 1.21 - 1.84 (10 H, m), 0.91 (3 H, t, J = 6.2 Hz), 0.76 (1 H, m), 0.46 (2 H, m), 0.06 (2 H, m); MS (ESI): 432 (M+H), 455 (M+Na), 430 (M-H).

Example 2

(3S)-3-[(1-oxo-2-propyloctyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one

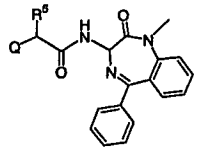


In accordance with Scheme 7, a mixture of acid **6** (186 mg, 1.00 mmol) and the (+)-camphorsulfonate salt of 3-(S)-amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one, **2**, (Paul J. Reider et al J. Org. Chem. 1987, 52, 955) (497 mg, 1.00 mmol) in 2 mL of methylene chloride was stirred at 0 °C. 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (383 mg, 2.00mmol) and triethylamine (0.17 mL, 1.2 mmol) were added sequentially (Scheme 7). After the mixture was stirred for 16 h, 30 mL

of ethyl acetate was added. The organic layer was washed with saturated aqueous Na_2CO_3 (30 mL) and brine (30 mL), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Purification by chromatotron (Harrison Research, Model 8924) (15% ethyl acetate - hexane) afforded two diastereomers **7a** and **7b**. A: 90 mg (21%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 - 7.65 (10 H, m), 5.58 (1 H, d, J = 8.5 Hz), 3.47 (3 H, s), 2.28 (1 H, m), 1.20 - 1.80 (14 H, m), 0.96 (3 H, t, J = 7.0 Hz), 0.87 (3 H, t, J = 6.3 Hz); MS (ESI): 434 (M+H), 456 (M+Na), 432 (M-H); B: 96 mg (22%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 - 7.65 (10 H, m), 5.59 (1 H, d, J = 8.4 Hz), 3.47 (3 H, s), 2.28 (1 H, m), 1.20 - 1.80 (14 H, m), 0.91 (6 H, m); MS (ESI) 434 (M+H), 456 (M+Na), 432 (M-H).

Table 1 below provides representative Examples of the compounds of the present invention. The compounds of Table 1 were prepared by methods disclosed herein using appropriate reagents.

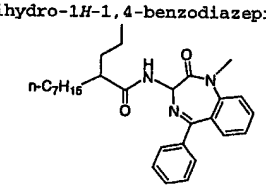
Table 1



Example	Q	R5	MS
3	n-heptyl	n-propyl	448.3 (M+H)
4	n-hexyl	n-butyl	470 (M+Na)
5	n-hexyl	methyl	392.3 (M+H)
6	n-pentyl	n-pentyl	448.3 (M+H)
7	n-propyl	n-propyl	805.3 (2M+Na)
8	n-propyl	methyl	364 (M+H)

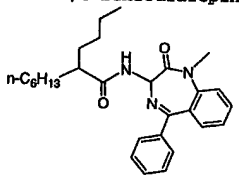
Example 3

(3S)-3-[(1-oxo-2-propylnonanyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one



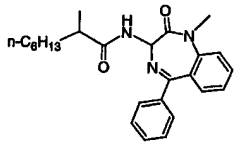
Example 4

(3S)-3-[(1-oxo-2-butyloctyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one



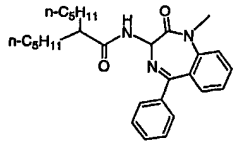
Example 5

(3S)-3-[(1-oxo-2-methyloctyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one



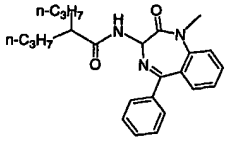
Example 6

(3S)-3-[(1-oxo-2-pentylheptanyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one



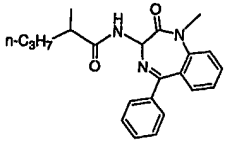
Example 7

(3S)-3-[(1-oxo-2-propylpentyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one



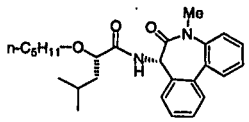
Example 8

(3S)-3-[(1-oxo-2-methylpentyl)amino]-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one



Example 9

(7S)-[(2S)-1-oxo-2-pentyloxy-4-methylpentyl]amino-5-methyl-5H,7H-dibenzo[b,d]azepin-6-one



Step 1': Preparation of (2S)-pentyl 4-methyl-2-pentyloxypentanoate **9** (Scheme 8). To a solution of (2S)-2-hydroxy-4-methylpentanoic acid **8** (1 g, 7.6 mmol) in 50 mL DMF at 0 °C was added NaH (0.6 g, 15.2 mmol) and stirred for 20 min, followed by the addition of iodopentane (1.5 g, 7.6 mmol). The reaction mixture was stirred at rt for additional 16 h. The solution was poured into water and the layers separated. The aqueous layer was extracted with methylene chloride and the combined extracts were washed with sat'd $NaHCO_3$, dried over magnesium sulfate, and concentrated to a crude product. Upon further purification, compound **9** was obtained as an oil (80 mg, 4%). MS $[M + H]^+$ 273.

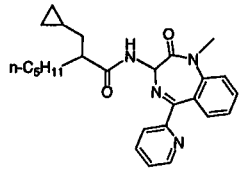
Step 2': Preparation of (2S)-4-methyl-2-pentyloxypentanoic acid **10**. To a solution of (2S)-pentyl 4-methyl-2-pentyloxypentanoate **9** (80 mg, 0.3 mmol) in 20 mL of THF cooled to 0 °C was added dropwise a solution of lithium hydroxide monohydrate (25 mg, 0.6 mmol) in 5 mL of water. The reaction mixture was stirred at rt for 16 h. THF was removed under reduced pressure to give an yellow oil which was diluted with 10 mL of 1 N HCl. The aqueous phase was extracted with CH_2Cl_2 (8 x 15 mL), and the extracts were combined, dried over Na_2SO_4, and concentrated to afford compound **10** (45mg, 74%). MS $[M + H]^+$ 203.

Step 3': Preparation of (7S)-[(2S)-1-oxo-2-pentyloxy-(4-methylpentyl)]amino-5-methyl-5H,7H-dibenzo[b,d]azepin-6-one, **12**. To a solution of (2S)-4-methyl-2-pentyloxypentanoic acid **10** (45 mg, 0.22 mmol) in CH_2Cl_2/DMF (5:1, 15 mL) at 0 °C was added HOBT (40 mg, 0.26 mmol) and EDC (50 mg, 0.26 mmol). The mixture was stirred for 10 min

then the amine **11** (52 mg, 0.22 mmol) was added and stirring was continued for 1 h. The solution was poured into water and the layers separated. The aqueous layer was extracted with methylene chloride and the combined extracts were washed with water, 1 N HCl, sat'd $NaHCO_3$, dried over magnesium sulfate, and concentrated to a glassy solid compound **12** (80 mg, 86%). MS $[M + H]^+$ 423.

Example 10.

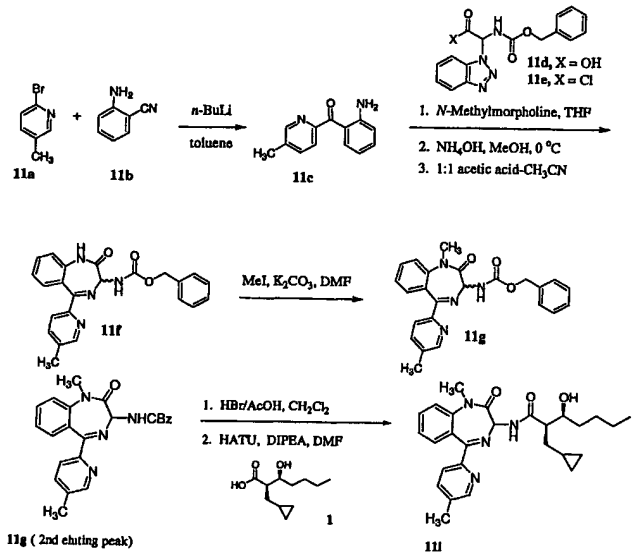
3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-(pyridin-2-yl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one.

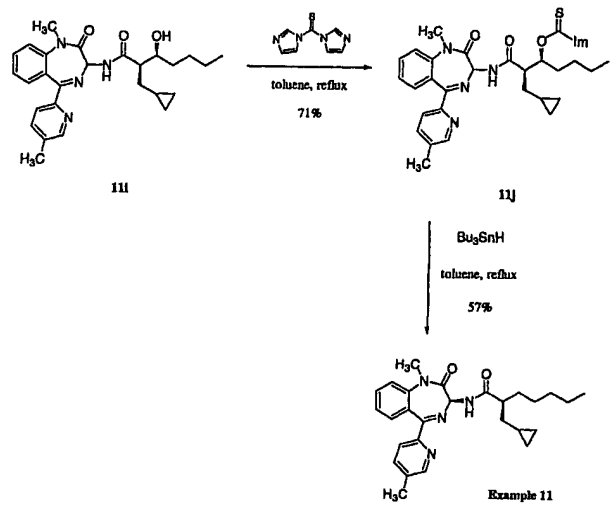


(±)-3-(2-(R)-Cyclopropylmethyl-3-(S)-hydroxyl-1-oxoheptyl)amino-1-methyl-5-(pyridin-2-yl)-2,3-dihydro-1H-1,4-benzodiazepin-2-one was made from **1** and 3-amino-1-methyl-5-(pyridin-2-yl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one (G. Semple et al Synth. Commun. 1996, 26, 721) according to **step 1** in **Example 1**.MS (ESI): 449 (M+H), 471 (M+Na), 447 (M-H). This diastereomeric mixture was submitted to chiral separation on a Chiralpak AD column with 10 - 15% i-propanol/hexane. The 2nd eluting peak was converted to **Example 10** by the same procedures of **steps 2** and **3** in **Example 1**. MS (ESI): 433.3 (M+H).

Example 11.

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-[4-methyl(pyridin-2-yl)]-2,3-dihydro-1H-1,4-benzodiazepin-2-one.





Step 1: A solution of 2-bromo-5-picoline **11a** (19.8 g, 115 mmol) and 2-cyanoaniline **11b** (8 g, 68 mmol) in toluene (80 mL) was cooled to -40 °C and treated with 2.5 M *n*-BuLi (102 mL, 253 mmol). After the addition, the reaction was warmed to 0 °C and stirred for 4.5 h. The reaction mixture was poured into 3 N HCl (75 mL) and stirred for 15 min. The organic portion was separated and extracted with 3 N HCl (25 mL). The aqueous portions were washed with toluene (25 mL) and made basic by the addition of 25% NaOH. The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The organic layers were combined and dried over $MgSO_4$. The solids were filtered and the solvent was removed under reduced pressure to afford **11c** as a dark red oil (4.8 g, 30%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.50 (m, 1 H), 7.70-7.60 (m, 3 H), 7.25 (m, 1 H), 6.70 (m, 1 H), 6.60 (m, 1 H), 6.20 (s, 2 H), 2.35 (s, 3 H).

Step 2: Acid **11d** (21g, 64 mmol) was dissolved in THF (190 mL) and cooled to 0 °C. The solution was treated with catalytic DMF (0.25 mL) and oxalyl chloride (5.5 mL, 64 mmol). After 2 h, amine **11c** (9 g, 42 mmol) and *N*-methylmorpholine (12 mL, 106 mmol) in THF (25 mL) were added slowly to the stirred reaction mixture. The reaction was warmed to rt and stirred for 12 h. The reaction was quenched by addition of H_2O (200 mL). The aqueous layer was extracted with CH_2Cl_2 (200 mL). The organic layer was washed with sat. $NaHCO_3$ (100 mL) and dried over $MgSO_4$. The solids were filtered and the solvent was removed under reduced pressure. The crude material was purified by SiO_2 column chromatography eluting with 3:6.8:0.2 Et_2O-CH_2Cl_2-Et_3N. The intermediate (10 g, 19 mmol) was dissolved in CH_3CN (130 mL) and cooled to 0 °C. The solution was treated with NH_3 which was bubbled through the reaction vessel for 20 min. A yellow solid precipitated from the solution. The reaction was slowly warmed to rt and stirred for 6 h. The excess NH_3 and CH_3CN was removed under reduced pressure. The solid material was transferred into a flask containing CH_3CN (100 mL) and acetic acid (200 mL) and stirred for 12 h at rt. The solvent was removed under reduced pressure. The material was dissolved in CH_2Cl_2 and washed with 5% NH_4OH in H_2O (100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude material was dissolved in CH_2Cl_2 (35 mL) and Et_2O (100 mL) was added via an addition funnel. A white solid precipitated from the solution. The solids were filtered and dried under reduced pressure to afford **11f** as a white solid (5.4 g, 64% from **11c**): ^1H NMR (300 MHz, $CDCl_3$) δ8.40 (m, 1 H), 8.38 (m, 1 H), 7.96 (m, 1 H), 7.45-7.20 (m, 8 H), 7.15 (m, 1 H), 6.95 (m, 1 H), 5.35 (m, 1 H), 5.14 (m, 2 H), 2.39 (s, 3 H).

Step 3: A solution of intermediate **11f** (5.4 g, 13.4 mmol) and finely ground K_2CO_3 (12.9 g, 94 mmol) in DMF (20 mL)

was warmed to 50 °C. To the solution was added MeI (1.3 mL, 20 mmol). After 2-3 h, the DMF was removed under reduced pressure. The crude material was dissolved in EtOAc (75 mL) and washed with H_2O (3 x 50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford **11g** as a yellow solid (3.8 g, 68%): mp 157-158 °C; ^1H NMR (500 MHz, $CDCl_3$) δ8.42 (m, 1 H), 8.05 (m, 1 H), 7.55 (m, 2 H), 7.43-7.20 (m, 8 H), 6.70 (m, 1 H), 5.36 (m, 1 H), 5.13 (m, 2 H), 3.42 (s, 3 H), 2.38 (s, 3 H); IR (CH_2Cl_2) 3054, 1726, 1682, 1499, 1266, 1069, 739, 704 cm^{-1}; FAB MS *m/z* = 415 $[C_{24}H_{22}N_4O_3+H]^+$; HPLC 96.8% t_r = 17.23 min. using HPLC condition A.

Step 4: (±)-**11g** was submitted to chiral separation on a CHIRALCEL OD column with 1/300/700 ratio of diethylamine/EtOH/CO_2. Only the 2nd eluting peak was used in the next step.

Step 5: To a solution of the product of **Step 4** (0.92 g, 2.2 mmol) in CH_2Cl_2 (11 mL) was added HBr (2.2 mL, 30% in acetic acid) and the reaction was stirred 4 h. The reaction was concentrated and azeotroped with toluene (4 x 15 mL) to obtain an orange solid. The crude reaction material was dissolved in DMF (20 mL) followed by addition of acid **1** (0.44 g, 2.2 mmol), HATU (0.84 g, 2.2 mmol) and diisopropylethylamine (1.9 mL, 11 mmol). After stirring for 14 h the reaction was quenched by addition of H_2O and ethyl acetate. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over sodium sulfate and concentrated under reduced pressure. The crude raction was purified by column chromatography (ethyl acetate) to afford **11i** (0.28 g, 29% for two steps) as a white solid: mp 84-102; ^1H NMR (500 MHz, CD_3OD) δ8.36 (d, J = 1.4 Hz, 1 H), 7.93 (d, J = 8.1 Hz, 1 H), 7.77 (m, 1 H), 7.65 (m, 1 H), 7.59 (m, 1 H), 7.28 (m, 2 H), 5.47 (s, 1 H), 3.65 (m, 1H),

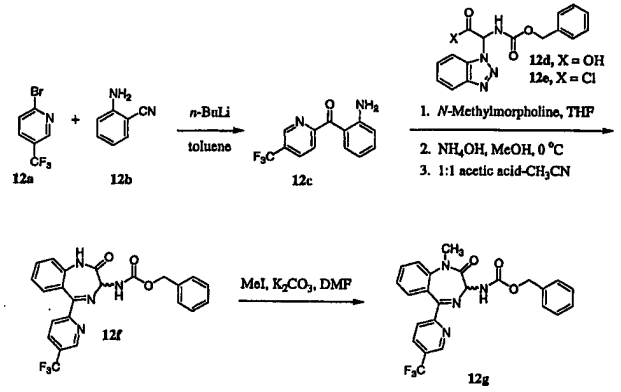
3.45 (s, 3 H), 2.59 (m, 1 H), 2.41 (s, 3 H), 1.56-1.32 (m, 8 H), 0.92 (t, J = 7 Hz, 3 H), 0.79 (m, 1 H), 0.43 (m, 2 H), 0.07 (m, 2H) ; IR (KBr) 3422, 2930, 1669, 1448 cm^{-1}; API MS m/z = 463 [$C_{27}H_{34}N_4O_3$+H]; HPLC >95%, t_r = 12.19 min. using HPLC condition A.

Step 6: To a solution of **11i** (0.17 g, 0.4 mmol) in dichloroethane (5 mL) was added 1,1'-thiocarbonyldiimidazole (0.26 g, 1.5 mmol) in dichloroethane (2 mL) and the reaction was heated to 80 °C for 12 h. After cooling, the reaction was concentrated and purified by column chromatography (ethyl acetate) to afford **11j** (0.17 g, 71%) as a pale yellow solid: ^{1}H NMR (500 MHz, CD_3OD) δ 8.52 (s, 1 H), 8.36 (s, 1H), 7.92 (d, J = 8.1 Hz, 1 H), 7.84 (t, J = 1.5 Hz, 1 H) 7.77 (m, 1 H), 7.65 (m, 1 H), 7.59 (m, 1 H), 7.30 (m, 2 H), 7.01 (s, 1H), 5.97 (m, 1H), 5.48 (s, 1 H), 3.45 (s, 3 H), 3.29 (m, 1H), 2.41 (s, 3 H), 2.01-1.79 (m, 3 H), 1.48-1.25 (m, 5 H), 0.91 (t, J = 6.8 Hz, 3 H), 0.80 (m, 1 H), 0.44 (m, 2 H), 0.08 (m, 2H).

Step 7: A solution of **11j** (0.17 g, 0.3 mmol) in toluene (5 mL) was heated to relux and then tributyltin hydride (0.13 mL, 0.5 mmol) in toluene (2 mL) was added dropwise. After 1 h the reaction was cooled and concentrated followed by column chromatography (hexanes, then 50:50 hexanes/ethyl acetate, then 5:95 methanol/methylene chloride) to afford **Example 11** (0.075 g, 57%) as a white solid: mp 71-89 °C; ^{1}H NMR (500 MHz, CD_3OD) • 8.38 (m, 1 H), 7.96 (d, J = 8.1 Hz, 1 H), 7.77 (m, 1 H), 7.65 (m, 1 H), 7.59 (m, 1 H), 7.30 (m, 2 H), 5.49 (s, 1 H), 3.48 (s, 3 H), 2.62 (m, 1 H), 2.41 (s, 3 H), 1.56-1.32 (m, 11 H), 0.92 (m, 3 H), 0.79 (m, 1 H), 0.45 (m, 2 H), 0.08 (m, 2H); IR (KBr) 3423, 2928, 1664, 1498 cm^{-1}; ES MS m/z = 447 [$C_{27}H_{34}N_4O_2$+H]; HPLC >95%, t_r = 20.27 min. using HPLC condition A.

Example 12.

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-[4-trifluoromethyl(pyridin-2-yl)]-2,3-dihydro-1H-1,4-benzodiazepin-2-one.



Step 1: **12c** was prepared from **12a** and **12b** by the same method as shown for **11c**. Compound **12c** was isolated as a brown oil (6.6 g, 61%): ^{1}H NMR δ 8.95 (s, 1 H), 8.09 (m, 1 H), 7.85 (m, 1 H), 7.55 (m, 1 H), 7.30 (m, 1 H), 6.72 (m, 1 H), 6.61 (m, 1 H), 6.35 (m, 2 H).

Step 2: Acid **12d** (13 g, 39 mmol) was dissolved in THF (100 mL) and cooled to 0 °C. The solution was treated with catalytic DMF (0.25 mL) and oxalyl chloride (3.4 mL, 39 mmol). After 2 h, amine **12c** (6.6 g, 26 mmol) and N-methylmorpholine (7.2 mL, 65 mmol) in THF (31 mL) were added slowly to the stirred reaction mixture. The reaction was warmed to rt and stirred for 12 h. The reaction was quenched by addition of H_2O (200 mL). The aqueous layer was extracted with CH_2Cl_2 (200 mL). The organic layer was washed with sat. $NaHCO_3$ (100 mL) and dried over $MgSO_4$. The solids were filtered and the solvent was removed under reduced pressure. The crude material was purified by SiO_2 column chromatography eluting with 1:4 Et_2O-CH_2Cl_2. The

intermediate (7.8 g, 14 mmol) was dissolved in CH_3CN (95 mL) and cooled to 0 °C. The solution was treated with NH_3, which was bubbled through the reaction vessel for 20 min. The reaction was slowly warmed to rt and stirred for 6 h. The excess NH_3 and CH_3CN was removed under reduced pressure. The solid material was dissolved in 1:2 CH_3CN-acetic acid (210 mL) and stirred for 12 h at rt. The solvent was removed under reduced pressure. The material was dissolved in CH_2Cl_2 and washed with 5% NH_4OH in H_2O (100 mL) and then brine (100 mL). The organic later was dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude material was purified by SiO_2 column chromatography eluting with 1:3 EtOAc-CH_2Cl_2 to provide the product as a dark blue amorphous solid. To the solid material was added 25% EtOAc-hexane. The solids were filtered to give **12f** as a light blue solid (2.8 g, 44%): ^1H NMR (300 MHz, $CDCl_3$) δ8.83 (m, 1 H), 8.25 (m, 1 H), 8.07 (s, 1 H), 8.04 (m, 1 H), 7.56 (m, 1 H), 7.42-7.22 (m, 6 H), 7.24 (m, 1 H), 7.13 (m, 1 H), 6.62 (m, 1 H), 5.45 (m, 1 H), 5.17 (m, 2 H).

Step 3: A solution of intermediate **12f** (3.4 g, 7.6 mmol) and finely ground K_2CO_3 (7.3 g, 53 mmol) in DMF (11 mL) was warmed to 50 °C. To the solution was added MeI (0.71 mL, 11 mmol). After 2-3 h, the DMF was removed under reduced pressure. The crude material was dissolved in EtOAc (250 mL) and washed with H_2O (2 x 150 mL), 5% LiCl (50 mL) and brine (150 mL). The organic layer was dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude material was dissolved in 3 mL of CH_2Cl_2 and then diluted with 100 mL of 1:1 Et_2O-Hexane followed by 200 mL of hexane. The resulting solid was further purified by SiO_2 column chromatography eluting with 50:40:10 EtOAc-Hexane-THF to afford **12g** as an off white solid (1.9 g, 55%): mp 179-180 °C; ^1H NMR (500 MHz, $CDCl_3$) δ8.85 (s, 1 H), 8.32 (m, 1 H), 8.03 (m, 1 H), 7.60 (m, 1 H), 7.40-7.20 (m, 8 H), 6.74 (m, 1 H), 5.41 (m, 1 H), 5.15 (m, 2 H), 3.46

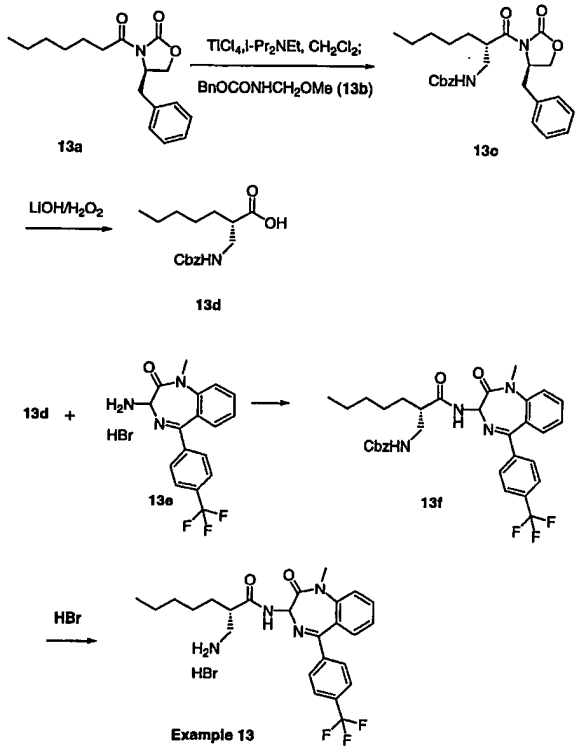
(s, 3 H); IR (KBr) 3422, 1723, 1687, 1604, 1498, 1324, 1131, 1079, 1016 cm^{-1}; CI MS *m/z* = 469 $[C24H19F3N4O3+H]^+$; HPLC >95% t_r = 20.39 min. using HPLC condition A.

Step 4: (±)-**Example 12** was submitted to chiral separation on a CHIRALPAK AD column with acetonitrile. Only the 1st eluting peak was used in the next steps.

Using the product of **step 4**, the title compound was made according to the procedures in **Steps 5, 6 and 7** of **Example 11**. MS (ESI): 501 (M+H).

Example 13.

3-[1-oxo-2-(S)-aminomethyl-heptyl]amino-1-methyl-(5-trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one hydrobromide.



Step 1: 13a (1.07 g, 3.7 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) and cooled to -60 °C. $TiCl_4$ was added dropwise via a cannula to the above solution, followed by addition of diisopropylethylamine (0.68 mL, 3.9 mmol). After stirring for 1 h at -60 °C, the resulting mixture was added a solution of *N*-methoxymethyl benzyl carbamate (**13b**, 0.94 g, 4.8 mmol) in CH_2Cl_2 (5 mL) via cannula. The reaction mixture was allowed to warm up to 0 °C in 1 h, quenched with saturated NH_4Cl (aq), and extracted with CH_2Cl_2 (3 x 20 mL). The extracts were combined, washed

with $NaHCO_3$ (sat'd), brine, dried ($MgSO_4$), filtered, and concentrated. The residue was purified on silica gel, using 20% EtOAc-hexane, to afford **13c** (690 mg, 41%) as a colorless oil. MS *m/z* 453.4 (MH^+).

Note: *N*-methoxymethyl benzyl carbamate was prepared according to C. J. Barnett et al Tetrahedron Lett. 1997, 38 (5), 735.

Titanium enolate used in the above reaction was generated according to D. A. Evans et al J. Am. Chem. Soc. 1990, 112, 8215.

Step 2: 13c (0.68 g, 1.5 mmol) was dissolved in THF (8 mL) and cooled to 0 °C. H_2O_2 (1.6 mL, 15 mmol) and an aqueous solution of LiOH (2 mL, 1.5 M) were added dropwise to the above solution sequentially at a rate of keeping the internal temperature below 10 °C. The resulting cloudy mixture was stirred at room temperature for 16 h, re-cooled to 0 °C, and quenched with aqueous Na_2SO_3 (4 mL, 1.5 M). The mixture was stirred for an additional 1 h, concentrated *in vacuo*, and washed with CH_2Cl_2 (3 x 10 mL). The aqueous mixture was cooled in an ice-water bath, acidified to pH 2 with 6 N HCl, and extracted with EtOAc (3 x 10 mL). The extracts were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo* to give **13d** (274 mg, 62%) as a white solid.

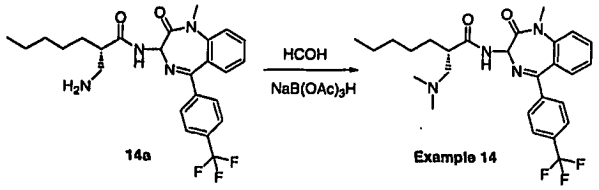
Step 4: 13d (270 mg, 0.92 mmol), **13e** (Note, 381 mg, 0.92 mmol), 1-hydroxybenzotriazole hydrate (HOBT, 149 mg, 1.10 mmol) were suspended in CH_2Cl_2 (4 mL) and cooled to 0 °C, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl, 353 mg, 1.84 mmol) and triethylamine (0.26 mL, 1.84 mmol) were added subsequently. After stirring for 24 h at ambient temperature, the reaction mixture was diluted with EtOAc (20 mL), washed with water, brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The residue was purified on silica gel (50% EtOAc/hexane) to afford **13f** (460 mg, 82%) as a white solid. MS *m/z* 609.5 (MH^+).

Note: (±)-**13e**, in Cbz protected form, was separated on a CHIRALPAK AD column with acetonitrile. Only the 1st eluting peak was converted, by the action of hydrogen bromide, to 3-amino-1-methyl-(5-trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one hydrobromide (**13e**)used in the above reaction.

Step 5: **13f** (200 mg, 0.33 mmol) was dissolved in a solution of HBr in AcOH (2 mL, 30%) and stirred for 2 h at room temperature. The resulting mixture was triturated with Et_2O. The precipitate was filtered under N_2, thoroughly washed with Et_2O, and dried overnight under high vacuum to afford **Example 13** (154 mg, 84%) as a white solid. MS (ESI) *m/z* 475.5 (MH^+-HBr), 553.4 ($(M-H)^-$).

Example 14.

3-[1-oxo-2-(S)-(dimethylamino)methyl-heptyl]amino-1-methyl-5-(trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one.

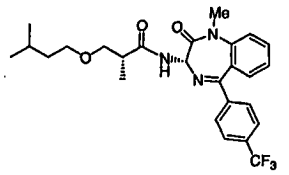


Formaldehyde (170 mg, 1.7 mmol, 37% aqueous solution) was added to a solution of **14a** (free base of **Example 13**, 80 mg, 0.17 mmol) and $NaBH(OAc)_3$ (107 mg, 0.51 mmol) in dichloroethane (1 mL) at room temperature. The resulting mixture was then vigorously stirred overnight, and extracted with EtOAc (3 x 10 mL). The extracts were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo*. The residue was purified on silica gel (1:5:100 Et_3N-CH_3OH-CH_2Cl_2) to afford **Example 14** (75

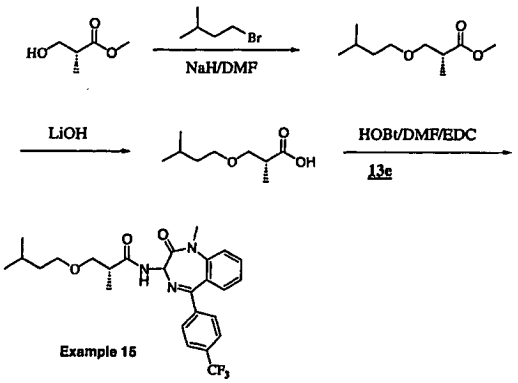
mg, 88%). ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7 Hz, 3 H), 1.20-1.45 (m, 7 H), 1.65-1.75 (m, 1 H), 2.23 (dd, *J* = 12, 4 Hz, 1 H), 2.32 (s, 6 H), 2.45-2.55 (m, 1 H), 2.72 (dd, *J* = 12, 11 Hz, 1H), 3.43 (s, 3 H), 5.58 (d, *J* = 8 Hz, 1 H), 7.18-7.35 (m, 3 H), 7.55-7.75 (m, 5 H), 9.21 (d, *J* = 8 Hz, 1 H); MS (ESI) *m/z* 503.5 (MH^+).

Example 15.

3-(3-isopentyloxy-2-(R)-methyl-1-oxo-propyl)amino-1-methyl-5-(trifluoromethyl)phneyl-2,3-dihydro-1H-1,4-benzodiazepin-2-one



The compound of Example 15 was prepared by methods disclosed herein using appropriate reagents.



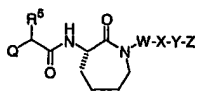
The racemic 3-amino-1-methyl-(5-trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one, in Cbz protected form, was separated on a CHIRALPAK AD column with acetonitrile. Only the 1st eluting peak was converted, by the action of hydrogen bromide, to an optically pure 3-amino-1-methyl-(5-trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one hydrobromide, which was used in the preparation of the title compound. MS (M+1) 490.

Table 2 demonstrates representative compounds envisaged within the scope of the present invention. Each formulae at the start of Table 2 are intended to be paired with each entry in the table which follows.

For example the compound (7S)-[(1-oxo-(2R)-2-methylpropyl-5-hexenyl)]-amino-5-methyl-5H,7H-dibenzo[b,d]azepin-6-one is represented by Example #500-B-j, which comprises the core B, side chain j, and entry #500.

For example the compound (3R)-[(1-oxo-(2S)-2-dimethylpropyl-5-pentenyl)]amino-7-chloro-1-methyl-5-phenyl-1,3-dihydro-benzo[e][1,4]diazepin-2-one is represented by Example #502-D-ab, which comprises the core D, side chain ab, and entry #502.

Table 2



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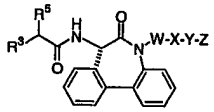

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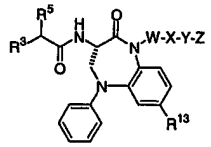

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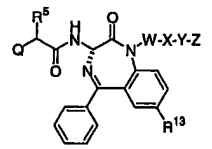

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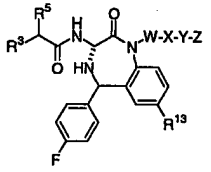

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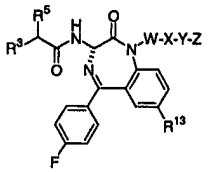

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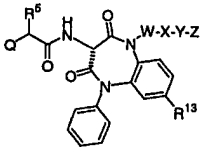

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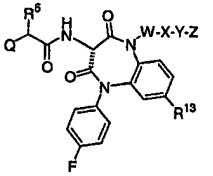

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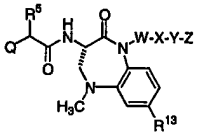

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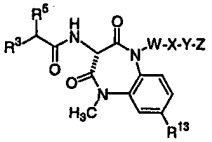
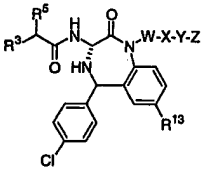
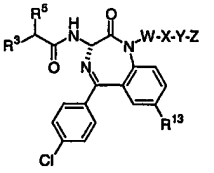


K





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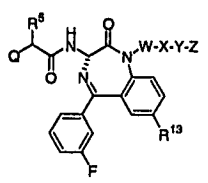

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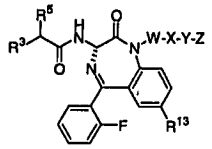

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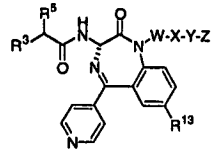

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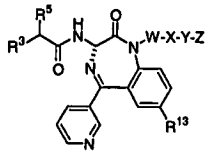

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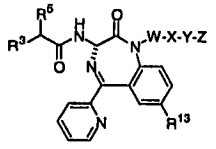
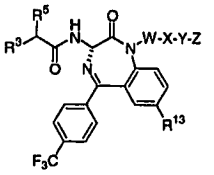


Q

R

S



wherein Q and R^5 are described, respectively, in the following moieties:

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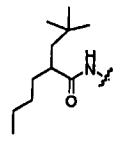

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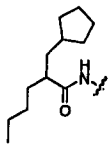

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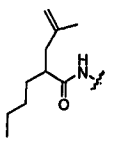

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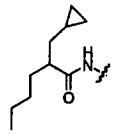

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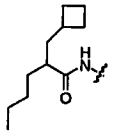

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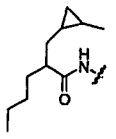

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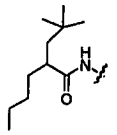

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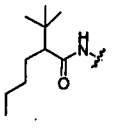

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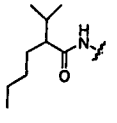

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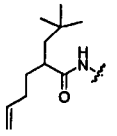

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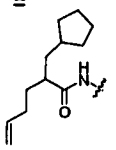

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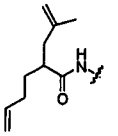

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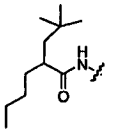

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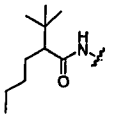

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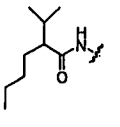

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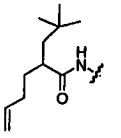

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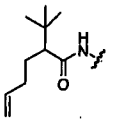

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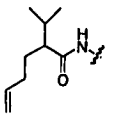

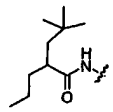
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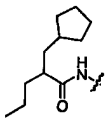
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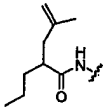
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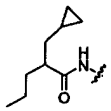
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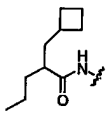
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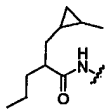
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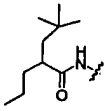
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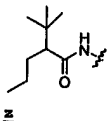
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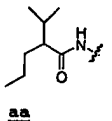
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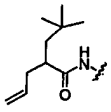
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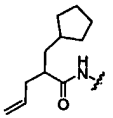
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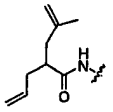
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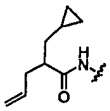
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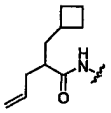
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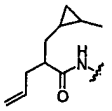
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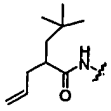
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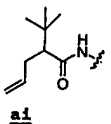
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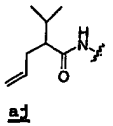
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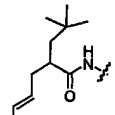
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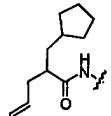
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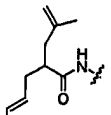
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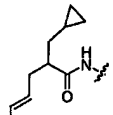
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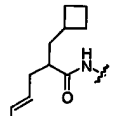
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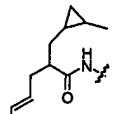
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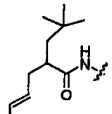
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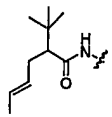
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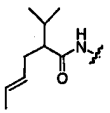
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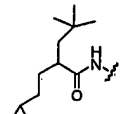
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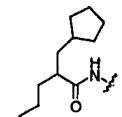
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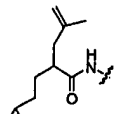
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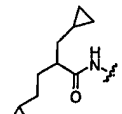
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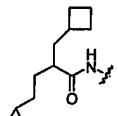
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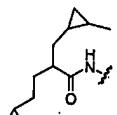
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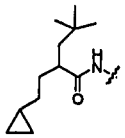

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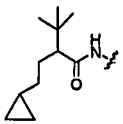

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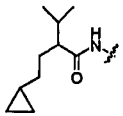

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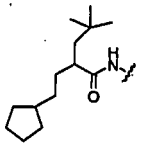

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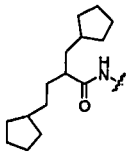

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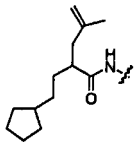

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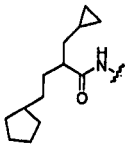

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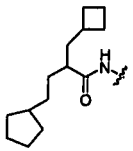

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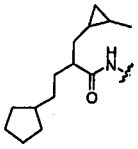

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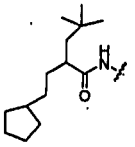

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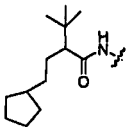

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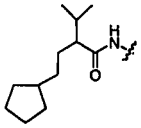

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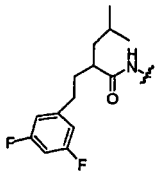

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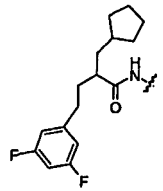

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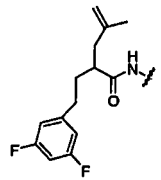

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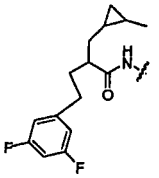

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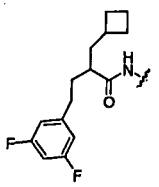

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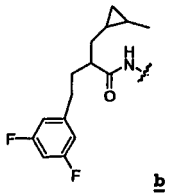

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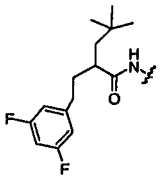

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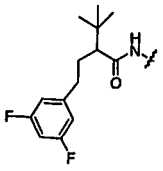

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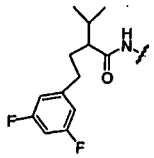

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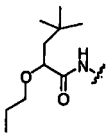

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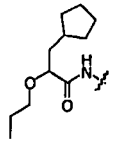

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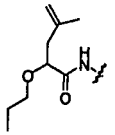

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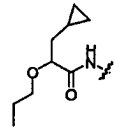

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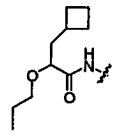

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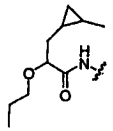

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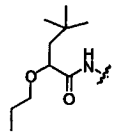

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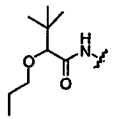

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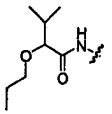

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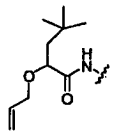

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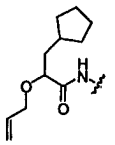

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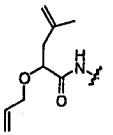

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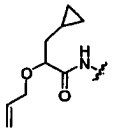

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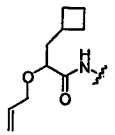

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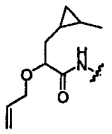

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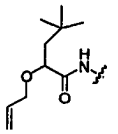

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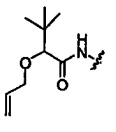

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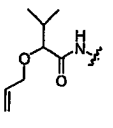

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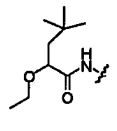

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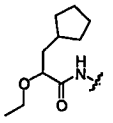

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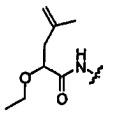

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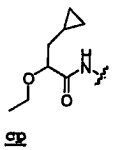

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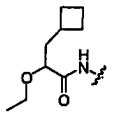

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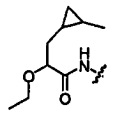

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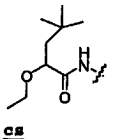

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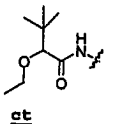

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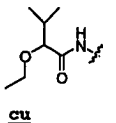

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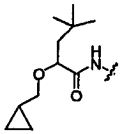

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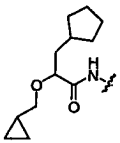

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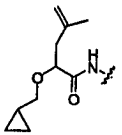

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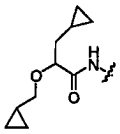

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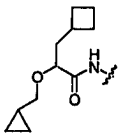

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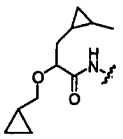

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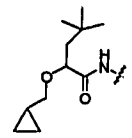

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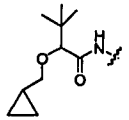

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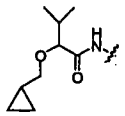

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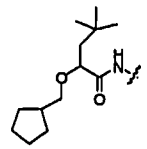

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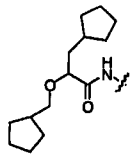

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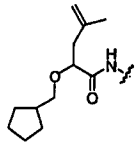

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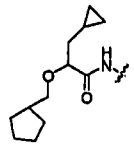

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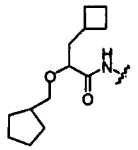

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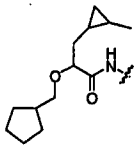

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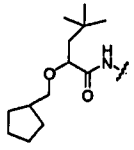

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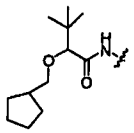

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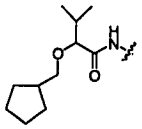

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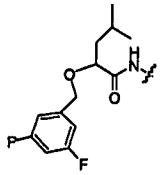

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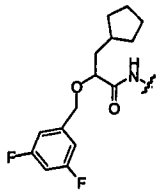

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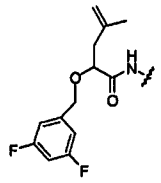

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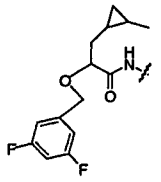

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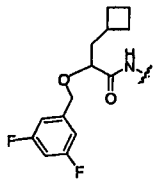

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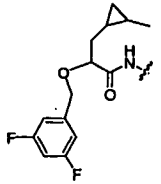

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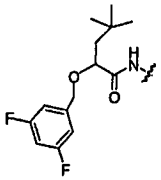

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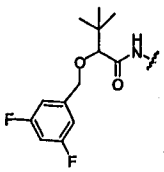

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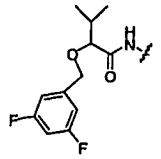


en

Table 2(cont.)

Ex#	core	Q/R5	R13	-W-X-Y-Z
500	A - S	a - en	H	methyl
501	A - S	a - en	F	methyl
502	A - S	a - en	Cl	methyl
503	A - S	a - en	OH	methyl
504	A - S	a - en	$-CH_3$	methyl
505	A - S	a - en	$-CH_2CH_3$	methyl
506	A - S	a - en	$-OCH_3$	methyl
507	A - S	a - en	$-CF_3$	methyl
508	A - S	a - en	H	ethyl
509	A - S	a - en	F	ethyl
510	A - S	a - en	Cl	ethyl
511	A - S	a - en	OH	ethyl
512	A - S	a - en	$-CH_3$	ethyl
513	A - S	a - en	$-CH_2CH_3$	ethyl
514	A - S	a - en	$-OCH_3$	ethyl

515	A - S	a - en	$-CF_3$	ethyl
516	A - S	a - en	H	i-propyl
517	A - S	a - en	F	i-propyl
518	A - S	a - en	Cl	i-propyl
519	A - S	a - en	OH	i-propyl
520	A - S	a - en	$-CH_3$	i-propyl
521	A - S	a - en	$-CH_2CH_3$	i-propyl
522	A - S	a - en	$-OCH_3$	i-propyl
523	A - S	a - en	$-CF_3$	i-propyl
524	A - S	a - en	H	n-propyl
525	A - S	a - en	F	n-propyl
526	A - S	a - en	Cl	n-propyl
527	A - S	a - en	OH	n-propyl
528	A - S	a - en	$-CH_3$	n-propyl
529	A - S	a - en	$-CH_2CH_3$	n-propyl
530	A - S	a - en	$-OCH_3$	n-propyl
531	A - S	a - en	$-CF_3$	n-propyl
532	A - S	a - en	H	n-butyl
533	A - S	a - en	F	n-butyl
534	A - S	a - en	Cl	n-butyl
535	A - S	a - en	OH	n-butyl
536	A - S	a - en	$-CH_3$	n-butyl
537	A - S	a - en	$-CH_2CH_3$	n-butyl
538	A - S	a - en	$-OCH_3$	n-butyl
539	A - S	a - en	$-CF_3$	n-butyl
540	A - S	a - en	H	i-butyl
541	A - S	a - en	F	i-butyl
542	A - S	a - en	Cl	i-butyl
543	A - S	a - en	OH	i-butyl
544	A - S	a - en	$-CH_3$	i-butyl
545	A - S	a - en	$-CH_2CH_3$	i-butyl
546	A - S	a - en	$-OCH_3$	i-butyl
547	A - S	a - en	$-CF_3$	i-butyl
548	A - S	a - en	H	s-butyl
549	A - S	a - en	F	s-butyl
550	A - S	a - en	Cl	s-butyl

551	A - S	a - en	OH	s-butyl
552	A - S	a - en	$-CH_3$	s-butyl
553	A - S	a - en	$-CH_2CH_3$	s-butyl
554	A - S	a - en	$-OCH_3$	s-butyl
555	A - S	a - en	$-CF_3$	s-butyl
556	A - S	a - en	H	t-butyl
557	A - S	a - en	F	t-butyl
558	A - S	a - en	Cl	t-butyl
559	A - S	a - en	OH	t-butyl
560	A - S	a - en	$-CH_3$	t-butyl
561	A - S	a - en	$-CH_2CH_3$	t-butyl
562	A - S	a - en	$-OCH_3$	t-butyl
563	A - S	a - en	$-CF_3$	t-butyl
564	A - S	a - en	H	allyl
565	A - S	a - en	F	allyl
566	A - S	a - en	Cl	allyl
567	A - S	a - en	OH	allyl
568	A - S	a - en	$-CH_3$	allyl
569	A - S	a - en	$-CH_2CH_3$	allyl
570	A - S	a - en	$-OCH_3$	allyl
571	A - S	a - en	$-CF_3$	allyl
572	A - S	a - en	H	cyclopropyl
573	A - S	a - en	F	cyclopropyl
574	A - S	a - en	Cl	cyclopropyl
575	A - S	a - en	OH	cyclopropyl
576	A - S	a - en	$-CH_3$	cyclopropyl
577	A - S	a - en	$-CH_2CH_3$	cyclopropyl
578	A - S	a - en	$-OCH_3$	cyclopropyl
579	A - S	a - en	$-CF_3$	cyclopropyl
580	A - S	a - en	$-CF_3$	cyclopropyl
581	A - S	a - en	H	cyclopropyl-CH_2-
582	A - S	a - en	F	cyclopropyl-CH_2-
583	A - S	a - en	Cl	cyclopropyl-CH_2-
584	A - S	a - en	OH	cyclopropyl-CH_2-
585	A - S	a - en	$-CH_3$	cyclopropyl-CH_2-
586	A - S	a - en	$-CH_2CH_3$	cyclopropyl-CH_2-

587	A - S	a - en	$-OCH_3$	cyclopropyl-CH_2-
588	A - S	a - en	$-CF_3$	cyclopropyl-CH_2-
589	A - S	a - en	H	cyclobutyl
590	A - S	a - en	F	cyclobutyl
591	A - S	a - en	Cl	cyclobutyl
592	A - S	a - en	OH	cyclobutyl
593	A - S	a - en	$-CH_3$	cyclobutyl
594	A - S	a - en	$-CH_2CH_3$	cyclobutyl
595	A - S	a - en	$-OCH_3$	cyclobutyl
596	A - S	a - en	$-CF_3$	cyclobutyl
597	A - S	a - en	H	cyclobutyl-CH_2-
598	A - S	a - en	F	cyclobutyl-CH_2-
599	A - S	a - en	Cl	cyclobutyl-CH_2-
600	A - S	a - en	OH	cyclobutyl-CH_2-
601	A - S	a - en	$-CH_3$	cyclobutyl-CH_2-
602	A - S	a - en	$-CH_2CH_3$	cyclobutyl-CH_2-
603	A - S	a - en	$-OCH_3$	cyclobutyl-CH_2-
604	A - S	a - en	$-CF_3$	cyclobutyl-CH_2-
605	A - S	a - en	H	cyclopentyl
606	A - S	a - en	F	cyclopentyl
607	A - S	a - en	Cl	cyclopentyl
608	A - S	a - en	OH	cyclopentyl
609	A - S	a - en	$-CH_3$	cyclopentyl
610	A - S	a - en	$-CH_2CH_3$	cyclopentyl
611	A - S	a - en	$-OCH_3$	cyclopentyl
612	A - S	a - en	$-CF_3$	cyclopentyl
613	A - S	a - en	H	cyclopentyl-CH_2-
614	A - S	a - en	F	cyclopentyl-CH_2-
615	A - S	a - en	Cl	cyclopentyl-CH_2-
616	A - S	a - en	OH	cyclopentyl-CH_2-
617	A - S	a - en	$-CH_3$	cyclopentyl-CH_2-
618	A - S	a - en	$-CH_2CH_3$	cyclopentyl-CH_2-
619	A - S	a - en	$-OCH_3$	cyclopentyl-CH_2-
620	A - S	a - en	$-CF_3$	cyclopentyl-CH_2-
621	A - S	a - en	H	cyclohexyl
622	A - S	a - en	F	cyclohexyl

623	A - S	a - en	Cl	cyclohexyl
624	A - S	a - en	OH	cyclohexyl
625	A - S	a - en	$-CH_3$	cyclohexyl
626	A - S	a - en	$-CH_2CH_3$	cyclohexyl
627	A - S	a - en	$-OCH_3$	cyclohexyl
628	A - S	a - en	$-CF_3$	cyclohexyl
629	A - S	a - en	H	cyclohexyl-CH_2-
630	A - S	a - en	F	cyclohexyl-CH_2-
631	A - S	a - en	Cl	cyclohexyl-CH_2-
632	A - S	a - en	OH	cyclohexyl-CH_2-
633	A - S	a - en	$-CH_3$	cyclohexyl-CH_2-
634	A - S	a - en	$-CH_2CH_3$	cyclohexyl-CH_2-
635	A - S	a - en	$-OCH_3$	cyclohexyl-CH_2-
636	A - S	a - en	$-CF_3$	cyclohexyl-CH_2-
637	A - S	a - en	H	phenyl
638	A - S	a - en	F	phenyl
639	A - S	a - en	Cl	phenyl
640	A - S	a - en	OH	phenyl
641	A - S	a - en	$-CH_3$	phenyl
642	A - S	a - en	$-CH_2CH_3$	phenyl
643	A - S	a - en	$-OCH_3$	phenyl
644	A - S	a - en	$-CF_3$	phenyl
645	A - S	a - en	H	2-F-phenyl
646	A - S	a - en	F	2-F-phenyl
647	A - S	a - en	Cl	2-F-phenyl
648	A - S	a - en	OH	2-F-phenyl
649	A - S	a - en	$-CH_3$	2-F-phenyl
650	A - S	a - en	$-CH_2CH_3$	2-F-phenyl
651	A - S	a - en	$-OCH_3$	2-F-phenyl
652	A - S	a - en	$-CF_3$	2-F-phenyl
653	A - S	a - en	H	3-F-phenyl
654	A - S	a - en	F	3-F-phenyl
655	A - S	a - en	Cl	3-F-phenyl
656	A - S	a - en	OH	3-F-phenyl
657	A - S	a - en	$-CH_3$	3-F-phenyl
658	A - S	a - en	$-CH_2CH_3$	3-F-phenyl

659	A - S	a - en	$-OCH_3$	3-F-phenyl
660	A - S	a - en	$-CF_3$	3-F-phenyl
661	A - S	a - en	H	4-F-phenyl
662	A - S	a - en	F	4-F-phenyl
663	A - S	a - en	Cl	4-F-phenyl
664	A - S	a - en	OH	4-F-phenyl
665	A - S	a - en	$-CH_3$	4-F-phenyl
666	A - S	a - en	$-CH_2CH_3$	4-F-phenyl
667	A - S	a - en	$-OCH_3$	4-F-phenyl
668	A - S	a - en	$-CF_3$	4-F-phenyl
669	A - S	a - en	H	3-Cl-phenyl
670	A - S	a - en	F	3-Cl-phenyl
671	A - S	a - en	Cl	3-Cl-phenyl
672	A - S	a - en	OH	3-Cl-phenyl
673	A - S	a - en	$-CH_3$	3-Cl-phenyl
674	A - S	a - en	$-CH_2CH_3$	3-Cl-phenyl
675	A - S	a - en	$-OCH_3$	3-Cl-phenyl
676	A - S	a - en	$-CF_3$	3-Cl-phenyl
677	A - S	a - en	H	4-Cl-phenyl
678	A - S	a - en	F	4-Cl-phenyl
679	A - S	a - en	Cl	4-Cl-phenyl
680	A - S	a - en	OH	4-Cl-phenyl
681	A - S	a - en	$-CH_3$	4-Cl-phenyl
682	A - S	a - en	$-CH_2CH_3$	4-Cl-phenyl
683	A - S	a - en	$-OCH_3$	4-Cl-phenyl
684	A - S	a - en	$-CF_3$	4-Cl-phenyl
685	A - S	a - en	H	3-Me-phenyl
686	A - S	a - en	F	3-Me-phenyl
687	A - S	a - en	Cl	3-Me-phenyl
688	A - S	a - en	OH	3-Me-phenyl
689	A - S	a - en	$-CH_3$	3-Me-phenyl
690	A - S	a - en	$-CH_2CH_3$	3-Me-phenyl
691	A - S	a - en	$-OCH_3$	3-Me-phenyl
692	A - S	a - en	$-CF_3$	3-Me-phenyl
693	A - S	a - en	H	4-Me-phenyl
694	A - S	a - en	F	4-Me-phenyl

695	A - S	a - en	Cl	4-Me-phenyl
696	A - S	a - en	OH	4-Me-phenyl
697	A - S	a - en	$-CH_3$	4-Me-phenyl
698	A - S	a - en	$-CH_2CH_3$	4-Me-phenyl
699	A - S	a - en	$-OCH_3$	4-Me-phenyl
700	A - S	a - en	$-CF_3$	4-Me-phenyl
701	A - S	a - en	H	3-MeO-phenyl
702	A - S	a - en	F	3-MeO-phenyl
703	A - S	a - en	Cl	3-MeO-phenyl
704	A - S	a - en	OH	3-MeO-phenyl
705	A - S	a - en	$-CH_3$	3-MeO-phenyl
706	A - S	a - en	$-CH_2CH_3$	3-MeO-phenyl
707	A - S	a - en	$-OCH_3$	3-MeO-phenyl
708	A - S	a - en	$-CF_3$	3-MeO-phenyl
709	A - S	a - en	H	4-MeO-phenyl
710	A - S	a - en	F	4-MeO-phenyl
711	A - S	a - en	Cl	4-MeO-phenyl
712	A - S	a - en	OH	4-MeO-phenyl
713	A - S	a - en	$-CH_3$	4-MeO-phenyl
714	A - S	a - en	$-CH_2CH_3$	4-MeO-phenyl
715	A - S	a - en	$-OCH_3$	4-MeO-phenyl
716	A - S	a - en	$-CF_3$	4-MeO-phenyl
717	A - S	a - en	H	3-F_3C-phenyl
718	A - S	a - en	F	3-F_3C-phenyl
719	A - S	a - en	Cl	3-F_3C-phenyl
720	A - S	a - en	OH	3-F_3C-phenyl
721	A - S	a - en	$-CH_3$	3-F_3C-phenyl
722	A - S	a - en	$-CH_2CH_3$	3-F_3C-phenyl
723	A - S	a - en	$-OCH_3$	3-F_3C-phenyl
724	A - S	a - en	$-CF_3$	3-F_3C-phenyl
725	A - S	a - en	H	4-F_3C-phenyl
726	A - S	a - en	F	4-F_3C-phenyl
727	A - S	a - en	Cl	4-F_3C-phenyl
728	A - S	a - en	OH	4-F_3C-phenyl
729	A - S	a - en	$-CH_3$	4-F_3C-phenyl
730	A - S	a - en	$-CH_2CH_3$	4-F_3C-phenyl

731	A - S	a - en	$-OCH_3$	4-F_3C-phenyl
732	A - S	a - en	$-CF_3$	4-F_3C-phenyl

UTILITY

Aβ production has been implicated in the pathology of Alzheimer's Disease (AD). The compounds of the present invention have utility for the prevention and treatment of AD by inhibiting Aβ production. Methods of treatment target formation of Aβ production through the enzymes involved in the proteolytic processing of β amyloid precursor protein. Compounds that inhibit β or γsecretase activity, either directly or indirectly, control the production of Aβ. Such inhibition of β or γsecretases reduces production of Aβ, and is expected to reduce or prevent the neurological disorders associated with Aβ protein, such as Alzheimer's Disease.

Cellular screening methods for inhibitors of Aβ production, testing methods for the *in vivo* suppression of Aβ production, and assays for the detection of secretase activity are known in the art and have been disclosed in numerous publications, including *J.Med.Chem.* **1999**, *42, 3889-3898*, PCT publication number WO 98/22493, EPO publication number 0652009, US patent 5703129 and US patent 5593846; all hereby incorporated by reference.

The compounds of the present invention have utility for the prevention and treatment of disorders involving Aβ production, such as cerebrovascular disorders.

Compounds of Formula (I) are expected to possess γ-secretase inhibitory activity. The γ-secretase inhibitory activity of the compounds of the present invention is demonstrated using assays for such activity, for example, using the assay described below. Compounds of the present invention have been shown to inhibit the activity of γ-secretase, as determined by the Aβ immunoprecipitation assay.

Compounds provided by this invention should also be useful as standards and reagents in determining the ability of a potential pharmaceutical to inhibit Aβ production. These would be provided in commercial kits comprising a compound of this invention.

As used herein "µg" denotes microgram, "mg" denotes milligram, "g" denotes gram, "µL" denotes microliter, "mL" denotes milliliter, "L" denotes liter, "nM" denotes nanomolar, "µM" denotes micromolar, "mM" denotes millimolar, "M" denotes molar, "nm" denotes nanometer, "SDS" denotes sodium dodecyl sulfate, and "DMSO" denotes dimethyl sulfoxide, and "EDTA" denotes ethylenediaminetetraacetic acid.

A compound is considered to be active if it has an IC_{50} or K_i value of less than about 100µM for the inhibition of Aβ production. Preferrably the IC_{50} or K_i value is less than about 10µM; more preferrably the IC_{50} or K_i value is less than about 0.1µM. Compounds of the present invention have been shown to inhibit Aβ protein production with an IC_{50} or K_i value of less than 100µM.

β amyloid precursor protein accumulation assay

A novel assay to evaluate the accumulation of Aβ protein was developed to detect potential inhibitors of secretase. The assay uses the N 9 cell line, characterized for expression of exogenous APP by immunoblotting and immunoprecipitation.

The effect of test compounds on the accumulation of Aβ in the conditioned medium is tested by immunoprecipitation. Briefly, N 9 cells are grown to confluency in 6-well plates and washed twice with 1 x Hank's buffered salt solution. The cells are starved in methionine/cysteine deficient media for 30 min, followed by replacement with fresh deficient media containing 150uCi S35 Translabel (Amersham). Test compounds dissolved in DMSO (final concentration 1%) are added together with the addition of radiolabel. The cells are incubated for 4 h at 37°C in a tissue culture incubator.

At the end of the incubation period, the conditioned medium is harvested and pre-cleared by the addition of 5 µl normal mouse serum and 50ul of protein A Sepharose (Pharmacia), mixed by end-over-end rotation for 30 minutes

at 4°C, followed by a brief centrifugation in a microfuge. The supernatant is then harvested and transferred to fresh tubes containing 5ug of a monoclonal antibody (clone 1101.1; directed against an internal peptide sequence in Aβ) and 50 µl protein A Sepharose. After incubation overnight at 4°C, the samples are washed three times with high salt washing buffer (50mM Tris, pH 7.5, 500mM NaCl, 5mM EDTA, 0.5% Nonidet P-40), three times with low salt wash buffer (50mM Tris, pH 7.5, 150mM NaCl, 5mM EDTA, 0.5% Nonidet P-40), and three times with 10mM Tris, pH 7.5. The pellet after the last wash is resuspended in SDS sample buffer (Laemmli, 1970) and boiled for 3 minutes. The supernatant is then fractionated on either 10-20% Tris/Tricine SDS gels or on 16.5% Tris/Tricine SDS gels. The gels are dried and exposed to X-ray film or analyzed by phosphorimaging. The resulting image is analyzed for the presence of Aβ polypeptides. The steady-state level of Aβ in the presence of a test compound is compared to wells treated with DMSO (1%) alone. A typical test compound blocks Aβ accumulation in the conditioned medium, and is therefore considered active, with an IC_{50} less than 100 µM.

C-Terminus β Amyloid Precursor Protein Accumulation Assay

The effect of test compounds on the accumulation of C-terminal fragments is determined by immunoprecipitation of APP and fragments thereof from cell lysates. N 9 cells are metabolically labeled as above in the presence or absence of test compounds. At the end of the incubation period, the conditioned medium are harvested and cells lysed in RIPA buffer (10 mM Tris, pH 8.0 containing 1% Triton X-100, 1% deoxycholate, 0.1% SDS, 150mM NaCl, 0.125% NaN_3). Again, lysates are precleared with 5ul normal rabbit serum / 50ul protein A Sepharose, followed by the addition of BC-1 antiserum (15µl;) and 50µl protein A Sepharose for 16 hours at 4°C. The immunoprecipitates are washed as above, bound proteins eluted by boiling in SDS sample buffer and fractionated by Tris/Tricine SDS-PAGE. After exposure to

X-ray film or phosphorimager, the resulting images are analyzed for the presence of C-terminal APP fragments. The steady-state level of C-terminal APP fragments is compared to wells treated with DMSO (1%) alone. A typical test compound stimulates C-terminal fragment accumulation in the cell lysates, and is therefore considered active, with an IC_{50} less than 100 μM.

Aβ Immunoprecipitation Assay

This immunoprecipitation assay is specific for γ secretase (i.e., proteolytic activity required to generate the C-terminal end of Aβ either by direct cleavage or generating a C-terminal extended species which is subsequently further proteolyzed). N 9 cells are pulse labeled in the presence of a reported γ secretase inhibitor (MDL 28170) for 1 h, followed by washing to remove radiolabel and MDL 28170. The media is replaced and test compounds are added. The cells are chased for increasing periods of times and A β is isolated from the conditioned medium and C-terminal fragments from cell lysates (see above). The test compounds are characterized whether a stabilization of C-terminal fragments is observed and whether Aβ is generated from these accumulated precursor. A typical test compound prevents the generation of Aβ out of accumulated C-terminal fragments and is considered active with an IC_{50} less than 100 μM.

Dosage and Formulation

The compounds of the present invention can be administered orally using any pharmaceutically acceptable dosage form known in the art for such administration. The active ingredient can be supplied in solid dosage forms such as dry powders, granules, tablets or capsules, or in liquid dosage forms, such as syrups or aqueous suspensions. The active ingredient can be administered alone, but is generally administered with a pharmaceutical carrier. A valuable treatise with respect to pharmaceutical dosage

forms is Remington's Pharmaceutical Sciences, Mack Publishing.

The compounds of the present invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions. Likewise, they may also be administered in intravenous (bolus or infusion), intraperitoneal, subcutaneous, or intramuscular form, all using dosage forms well known to those of ordinary skill in the pharmaceutical arts. An effective but non-toxic amount of the compound desired can be employed to prevent or treat neurological disorders related to β-amyloid production or accumulation, such as Alzheimer's disease and Down's Syndrome.

The compounds of this invention can be administered by any means that produces contact of the active agent with the agent's site of action in the body of a host, such as a human or a mammal. They can be administered by any conventional means available for use in conjunction with pharmaceuticals, either as individual therapeutic agents or in a combination of therapeutic agents. They can be administered alone, but generally administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage regimen for the compounds of the present invention will, of course, vary depending upon known factors, such as the pharmacodynamic characteristics of the particular agent and its mode and route of administration; the species, age, sex, health, medical condition, and weight of the recipient; the nature and extent of the symptoms; the kind of concurrent treatment; the frequency of treatment; the route of administration, the renal and hepatic function of the patient,and the effect desired. An ordinarily skilled physician or veterinarian can readily determine and prescribe the effective amount of the drug

required to prevent, counter, or arrest the progress of the condition.

Advantageously, compounds of the present invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three, or four times daily.

The compounds for the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal routes, using those forms of transdermal skin patches wall known to those of ordinary skill in that art. To be administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittant throughout the dosage regimen.

In the methods of the present invention, the compounds herein described in detail can form the active ingredient, and are typically administered in admixture with suitable pharmaceutical diluents, excipients, or carriers (collectively referred to herein as carrier materials) suitably selected with respect to the intended form of administration, that is, oral tablets, capsules, elixirs, syrups and the like, and consistent with conventional pharmaceutical practices.

For instance, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic, pharmaceutically acceptable, inert carrier such as lactose, starch, sucrose, glucose, methyl callulose, magnesium stearate, dicalcium phosphate, calcium sulfate, mannitol, sorbitol and the like; for oral administration in liquid form, the oral drug components can be combined with any oral, non-toxic, pharmaceutically acceptable inert carrier such as ethanol, glycerol, water, and the like. Moreover, when desired or necessary, suitable binders, lubricants, disintegrating agents, and coloring agents can also be incorporated into the mixture. Suitable binders include starch, gelatin, natural sugars such as glucose or β-lactose, corn

sweeteners, natural and synthetic gums such as acacia, tragacanth, or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants used in these dosage forms include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum, and the like.

The compounds of the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamallar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine, or phosphatidylcholines.

Compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide-phenol, polyhydroxyethylaspartamidephenol, or polyethyleneoxide-polylysine substituted with palmitoyl residues. Furthermore, the compounds of the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyglycolic acid, copolymers of polylactic and polyglycolic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacylates, and crosslinked or amphipathic block copolymers of hydrogels.

Gelatin capsules may contain the active ingredient and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the

atmosphere, or enteric coated for selective disintegration in the gastrointestinal tract.

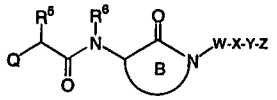
Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance. In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium EDTA. In addition, parenteral solutions can contain preservatives, such as benzalkonium chloride, methyl- or propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, Mack Publishing Company, a standard reference text in this field.

CLAIMS

What is claimed is:

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CR^7R^{7a})_m-R^4$,
$-(CR^7R^{7a})_n-S-R^4$,
$-(CR^7R^{7a})_n-O-R^4$,
$-(CR^7R^{7a})_m-N(R^{7b})-R^4$,
$-(CR^7R^{7a})_n-S(=O)-R^4$,
$-(CR^7R^{7a})_n-S(=O)_2-R^4$, or
$-(CR^7R^{7a})_n-C(=O)-R^4$;
provided when n is 0, then R^4 is not H;

m is 1, 2, or 3;

n is 0, 1, or 2;

R^4 is H,
C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, OR^{14a}, OR^{22}, SR^{22}, $C(=O)OR^{22}$, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from: H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^6 is H;
C_1-C_6 alkyl substituted with 0-3 R^{6a};
C_3-C_{10} carbocycle substituted with 0-3 R^{6b}; or
C_6-C_{10} aryl substituted with 0-3 R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, aryl or CF_3;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

R^7, at each occurrence, is independently H or C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently H or C_1-C_4 alkyl;

R^{7b} is H or C_1-C_4 alkyl;

Ring B is a 7 membered lactam,
wherein the lactam is saturated, partially saturated or unsaturated;
wherein each additional lactam carbon is substituted with 0-2 R^{11}; and,

optionally, the lactam contains a heteroatom selected from -O-, -S-, -S(=O)-, -S(=O)$_2$-, -N=, -NH-, and -N(R^{10})-;

additionally, two R^{11} substituents on adjacent atoms may be combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R^{13};

additionally, two R^{11} substituents on adjacent atoms may be combined to form a 5 to 6 membered heteroaryl fused radical, wherein said 5 to 6 membered heteroaryl fused radical comprises 1 or 2 heteroatoms selected from N, O, and S; wherein said 5 to 6 membered heteroaryl fused radical is substituted with 0-3 R^{13};

additionally, two R^{11} substituents on the same or adjacent carbon atoms may be combined to form a C_3-C_6 carbocycle substituted with 0-3 R^{13};

R^{10} is H, C(=O)R^{17}, C(=O)OR^{17}, C(=O)N$R^{18}R^{19}$, S(=O)$_2$N$R^{18}R^{19}$, S(=O)$_2R^{17}$;
C_1-C_6 alkyl optionally substituted with 0-3 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, N$R^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, N$R^{15}R^{16}$, CF_3, acetyl, SCH_3, S(=O)CH_3, S(=O)$_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{11}, at each occurrence, is independently selected from H, C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, N$R^{18}R^{19}$, C(=O)R^{17}, C(=O)OR^{17}, C(=O)N$R^{18}R^{19}$, S(=O)$_2$N$R^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with 0-3 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, N$R^{15}R^{16}$, CF_3;
phenyl substituted with 0-3 R^{11b};
C_3-C_6 cycloalkyl substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, N$R^{15}R^{16}$, CF_3, acetyl, SCH_3, S(=O)CH_3, S(=O)$_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

W is a bond or -(CR^8R^{8a})$_p$-;

p is 0, 1, 2, 3, or 4;

R^8 and R^{8a}, at each occurrence, are independently selected from H, F, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl and C_3-C_8 cycloalkyl;

X is a bond;

C_6-C_{10} aryl substituted with 0-3 R^{Xb};
C_3-C_{10} carbocycle substituted with 0-3 R^{Xb}; or
5 to 10 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 halothioalkoxy;

Y is a bond or $-(CR^9R^{9a})_t-V-(CR^9R^{9a})_u-$;

t is 0, 1, or 2;

u is 0, 1, or 2;

R^9 and R^{9a}, at each occurrence, are independently selected from H, F, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

V is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a};
C_2-C_6 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,

C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_6-C_{10} aryl substituted with 0-4 R^{12b}; C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, aryl, C_3-C_6 cycloalkyl, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-7 membered ring wherein said 4-7 membered ring optionally contains an additional heteroatom selected from O or NH;

R^{17} is H, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or $-CH_2$-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF_3, OCF_3, SCH_3, $S(O)CH_3$, SO_2CH_3, $-NH_2$, $-N(CH_3)_2$, or C_1-C_4 haloalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19b}, at each occurrence, is independently is H or C_1-C_4 alkyl;

R^{21} is H, phenyl, benzyl, or C_1-C_4 alkyl; and

R^{22} is C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_3-C_4 alkynyl.

2. A compound, according to Claim 1, of Formula (I) or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CR^7R^{7a})_m$-R^4, $-(CR^7R^{7a})_n$-S-R^4, $-(CR^7R^{7a})_n$-O-R^4, or $-(CR^7R^{7a})_m$-$N(R^{7b})$-R^4;

m is 1 or 2;

n is 0 or 1;

R^4 is H,
C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, OR^{14a}, $C(=O)OR^{22}$, SR^{22}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and

sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

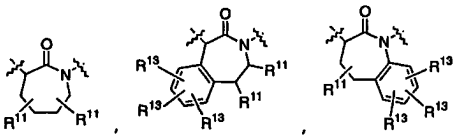
R^6 is H, methyl, or ethyl;

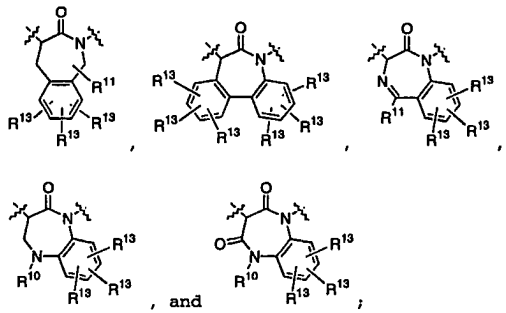
R^7, at each occurrence, is independently H or C_1-C_4 alkyl;

R^{7a}, at each occurrence, is independently H or C_1-C_4 alkyl;

R^{7b} is H or C_1-C_4 alkyl;

Ring B is selected from:





R^{10} is H, C(=O)R^{17}, C(=O)OR^{17}, C(=O)$NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;
C_1-C_6 alkyl optionally substituted with 0-3 R^{10a};
C_6-C_{10} aryl substituted with 0-4 R^{10b};
C_3-C_{10} carbocycle substituted with 0-3 R^{10b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{11}, at each occurrence, is independently selected from H, C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, $NR^{18}R^{19}$, C(=O)R^{17}, C(=O)OR^{17}, C(=O)$NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with 0-3 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3;
phenyl substituted with 0-3 R^{11b};
C_3-C_6 cycloalkyl substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

W is a bond or $-(CH_2)_p-$;

p is 1 or 2;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 carbocycle substituted with 0-2 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, and C_1-C_3 halothioalkoxy;

Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a};
C_2-C_6 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_6-C_{10} aryl substituted with 0-4 R^{12b}; C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-7 membered ring wherein said 4-7 membered ring optionally contains an additional heteroatom selected from O or NH;

R^{17} is H, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or -CH_2-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF_3, OCF_3, SCH_3, $S(O)CH_3$, SO_2CH_3, $-NH_2$, $-N(CH_3)_2$, or C_1-C_4 haloalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

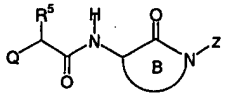
R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenethyl;

R^{19b}, at each occurrence, is independently is H or C_1-C_4 alkyl;

R^{21} is H, phenyl, benzyl, or C_1-C_4 alkyl; and

R^{22} is C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_3-C_4 alkynyl.

3. A compound, according to Claim 2, of Formula (Ib):



(Ib)

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CHR^7)_m-R^4$,
$-(CHR^7)_n-S-R^4$,
$-(CHR^7)_n-O-R^4$, or
$-(CHR^7)_m-N(R^{7b})-R^4$;

m is 1 or 2;

n is 0 or 1;

R^4 is H,
C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, OR^{14a}, $C(=O)OR^{22}$, SR^{22}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from: H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $R^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and

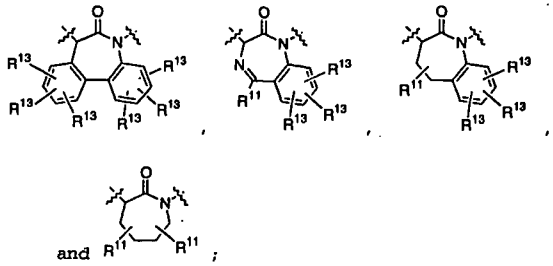
sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^7, at each occurrence, is independently H, methyl, or ethyl;

R^{7b} is H, methyl, or ethyl;

Ring B is selected from:



;

R^{11}, at each occurrence, is independently selected from H, C_1-C_4 alkoxy, Cl, F, Br, I, =O, CN, NO_2, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3;
C_1-C_6 alkyl optionally substituted with 0-3 R^{11a};
C_6-C_{10} aryl substituted with 0-3 R^{11b};
C_3-C_{10} carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, OR^{14}, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3;
phenyl substituted with 0-3 R^{11b};
C_3-C_6 cycloalkyl substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

W is a bond;
X is a bond;
Y is a bond;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a};
C_2-C_6 alkynyl substituted with 0-3 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_6-C_{10} aryl substituted with 0-4 R^{12b};

C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-7 membered ring wherein said 4-7 membered ring optionally contains an additional heteroatom selected from O or NH;

R^{17} is H, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, aryl substituted by 0-4 R^{17a}, or

-CH_2-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF_3, OCF_3, SCH_3, $S(O)CH_3$, SO_2CH_3, $-NH_2$, $-N(CH_3)_2$, or C_1-C_4 haloalkyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenethyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

4. A compound according to Claim 3 of Formula (I) or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Q is $-(CH_2)_m-R^4$,
$-(CH_2)_n-S-R^4$,
$-(CH_2)_n-O-R^4$, or
$-(CH_2)_m-N(H)-R^4$;

m is 1 or 2;

n is 0 or 1;

R^4 is C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},

C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{22}, OR^{14a}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_3-C_{10} carbocycle substituted with 0-3 R^{4b}, C_6-C_{10} aryl substituted with 0-3 R^{4b}, and 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

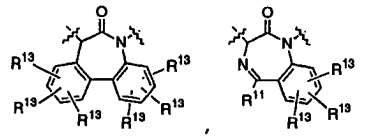
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5b}, at each occurrence, is independently selected from:
H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $R^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

Ring B is selected from: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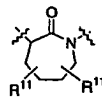
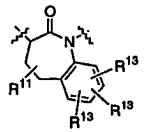

, and 
;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;
C_1-C_4 alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6

membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, F, Cl, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond;
X is a bond;
Y is a bond;

Z is H;
C_1-C_8 alkyl substituted with 0-3 R^{12a};
C_2-C_6 alkenyl substituted with 0-3 R^{12a}; or
C_2-C_6 alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, $-C(=O)NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-, C_6-C_{10} aryl substituted with 0-4 R^{12b}; C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b}; and wherein said 5 to 10 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl,

thiazolyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl;

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-; and

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-6 membered ring wherein said 4-6 membered ring optionally contains an additional heteroatom selected from O or NH, wherein said 4-6 membered ring is

selected from imidazolidinyl, oxazolidinyl, thiazolidinyl, piperazinyl, morpholinyl, and thiomorpholinyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenethyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

5. A compound according to Claim 4 wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-3 R^{4a}, C_2-C_6 alkenyl substituted with 0-3 R^{4a}, C_2-C_6 alkynyl substituted with 0-3 R^{4a}, C_3-C_6 carbocycle substituted with 0-3 R^{4b}, phenyl substituted with 0-3 R^{4b}, or 5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{14a}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,

C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

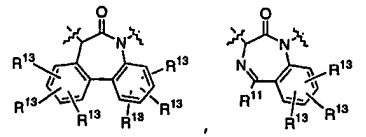
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b}; or
C_2-C_6 alkynyl substituted with 0-3 R^{5b};

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, Cl, F, Br, I, =O;
C_3-C_6 carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and
C_1-C_2 haloalkoxy;

Ring B is selected from: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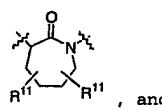
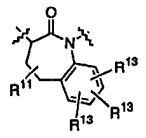

, and 
;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;
C_1-C_4 alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; and
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, phenoxy, F, Cl, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond;

X is a bond;
Y is a bond;

Z is H;
C_1-C_4 alkyl substituted with 0-3 R^{12a};
C_2-C_4 alkenyl substituted with 0-3 R^{12a}; or
C_2-C_4 alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, and benzyl;

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-$S(=O)_2$-, and ethyl-$S(=O)_2$-;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl;

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

6. A compound according to Claim 5 or a pharmaceutically acceptable salt or prodrug thereof wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-2 R^{4a},
C_2-C_6 alkenyl substituted with 0-2 R^{4a},
C_2-C_6 alkynyl substituted with 0-2 R^{4a}, or
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, OH, F, Cl, Br, I, CN, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, methoxy, ethoxy, propoxy, OCF_3;
C_3-C_6 carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

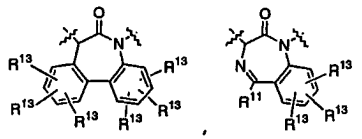
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

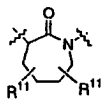
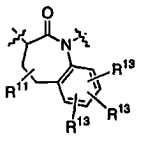
R^5 is H;
C_1-C_4 alkyl substituted with 0-1 R^{5b};
C_2-C_4 alkenyl substituted with 0-1 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-1 R^{5b};

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3;
C_3-C_6 carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Ring B is selected from:



, and ;

R^{11}, at each occurrence, is independently selected from

H, =O, $NR^{18}R^{19}$;
C_1-C_4 alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, methoxy, ethoxy, propoxy, phenoxy, F, Cl, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond;
X is a bond;
Y is a bond;

Z is H;
C_1-C_4 alkyl substituted with 0-1 R^{12a};
C_2-C_4 alkenyl substituted with 0-1 R^{12a}; or
C_2-C_4 alkynyl substituted with 0-1 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

R^{13}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R^{15}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl; and

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, and phenethyl;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl.

7. A compound according to Claim 6 wherein:

R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2NH_2$, $-CH_2N(CH_3)_2$, $-CH_2N(CH_2CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, or $-CH_2CH_2$-cyclohexyl;

Q is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl,

$-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, $-CH_2CH_2$-cyclohexyl, $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$, $-OCH(CH_3)_2$, $-OCH_2CH_2CH_2CH_3$, $-OCH_2CH(CH_3)_2$, $-OCH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH(CH_3)_2$, $-OCH_2$-cyclopropyl, $-OCH_2$-cyclobutyl, $-OCH_2$-cyclopentyl, $-OCH_2$-cyclohexyl, $-OCH_2CH_2$-cyclopropyl, $-OCH_2CH_2$-cyclobutyl, $-OCH_2CH_2$-cyclopentyl, $-OCH_2CH_2$-cyclohexyl, $-CH_2OCH_2CH_3$, $-CH_2OCH_2CH_2CH_3$, $-CH_2-OCH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH(CH_3)_2$, $-CH_2O$-cyclopropyl, $-CH_2O$-cyclobutyl, $-CH_2O$-cyclopentyl, $-CH_2O$-cyclohexyl, $-CH_2OCH_2$-cyclopropyl, $-CH_2OCH_2$-cyclobutyl, $-CH_2OCH_2$-cyclopentyl, $-CH_2OCH_2$-cyclohexyl; $-CH_2(NH)CH_3$, $-CH_2(NH)CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH_3$, $-CH_2-(NH)CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)$-cyclopropyl, $-CH_2(NH)$-cyclobutyl, $-CH_2(NH)$-cyclopentyl, $-CH_2(NH)$-cyclohexyl, $-CH_2(NH)CH_2$-cyclopropyl, $-CH_2(NH)CH_2$-cyclobutyl, $-CH_2(NH)CH_2$-cyclopentyl, or $-CH_2(NH)CH_2$-cyclohexyl;

W is a bond;

X is a bond;

Y is a bond;

Z is methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl, s-butyl, t-butyl, or allyl;

R^{11}, at each occurrence, is independently selected from H, =O, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-,

3-F-phenyl, (3-F-phenyl)CH_2-, (3-F-phenyl)CH_2CH_2-,
2-F-phenyl, (2-F-phenyl)CH_2-, (2-F-phenyl)CH_2CH_2-,
4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-,
3-Cl-phenyl, (3-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2CH_2-,
4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-,
3-CH_3-phenyl, (3-CH_3-phenyl)CH_2-, (3-CH_3-phenyl)CH_2CH_2-,
4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, (4-CF_3-phenyl)CH_2CH_2-,
pyrid-2-yl, 4-F-pyrid-2-yl, 4-Cl-pyrid-2-yl,
4-CH_3-pyrid-2-yl, 4-CF_3-pyrid-2-yl, pyrid-3-yl,
4-F-pyrid-3-yl, 4-Cl-pyrid-3-yl, 4-CH_3-pyrid-3-yl,
4-CF_3-pyrid-3-yl, or pyrid-4-yl; and

R^{13}, at each occurrence, is independently selected from H, F, Cl, OH, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, or $-CF_3$.

8. A compound according to Claim 2 of Formula (I) or a pharmaceutically acceptable salt or prodrug thereof wherein:

Q is $-(CH_2)_m-R^4$,
$-(CH_2)_n-S-R^4$,
$-(CH_2)_n-O-R^4$, or
$-(CH_2)_m-N(H)-R^4$;

m is 1 or 2;

n is 0 or 1;

R^4 is C_1-C_8 alkyl substituted with 0-3 R^{4a},
C_2-C_8 alkenyl substituted with 0-3 R^{4a},
C_2-C_8 alkynyl substituted with 0-3 R^{4a},
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{22}, OR^{14a}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,
C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl,
C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

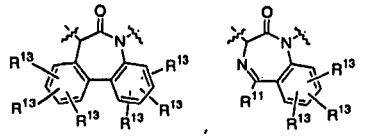
R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b};
C_2-C_6 alkynyl substituted with 0-3 R^{5b};
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

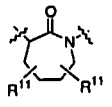
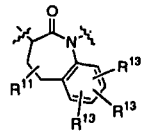
R^{5b}, at each occurrence, is independently selected from: H, C_1-C_6 alkyl, CF_3, Cl, F, Br, I, =O, CN, NO_2, $NR^{15}R^{16}$;
C_3-C_{10} carbocycle substituted with 0-3 R^{5c};
C_6-C_{10} aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

Ring B is selected from:



, and ;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;
C_1-C_4 alkyl optionally substituted with 0-3 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; and wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,

pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, OR^{14}, Cl, F, =O, CN, NO_2, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_4 haloalkoxy;

W is a bond, $-CH_2-$, $-CH_2CH_2-$;

X is a bond;
phenyl substituted with 0-2 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-2 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-2 R^{Xb};

R^{Xb}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-N(R^{19})-$, $-C(=O)NR^{19b}-$, $-NR^{19b}C(=O)-$, $-NR^{19b}S(=O)_2-$, $-S(=O)_2NR^{19b}-$, $-NR^{19b}S(=O)-$, $-S(=O)NR^{19b}-$, $-C(=O)O-$, or $-OC(=O)-$;

Z is C_1-C_3 alkyl substituted with 1-2 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_6 alkyl, C_2-C_6 alkoxyalkyl, or C_3-C_6 cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-;

R^{16}, at each occurrence, is independently selected from H, OH, C_1-C_6 alkyl, benzyl, phenethyl, (C_1-C_4 alkyl)-C(=O)-, and (C_1-C_4 alkyl)-$S(=O)_2$-; and

alternatively, R^{15} and R^{16}, together with the nitrogen to which they are attached, may combine to form a 4-6 membered ring wherein said 4-6 membered ring optionally contains an additional heteroatom selected from O or NH, wherein said 4-6 membered ring is

selected from imidazolidinyl, oxazolidinyl, thiazolidinyl, piperazinyl, morpholinyl, and thiomorpholinyl;

R^{18}, at each occurrence, is independently selected from H, C_1-C_6 alkyl, phenyl, benzyl, phenethyl, (C_1-C_6 alkyl)-C(=O)-, and (C_1-C_6 alkyl)-$S(=O)_2$-;

R^{19}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl;

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

9. A compound according to Claim 8 wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-3 R^{4a};
C_2-C_6 alkenyl substituted with 0-3 R^{4a};
C_2-C_6 alkynyl substituted with 0-3 R^{4a};
C_3-C_6 carbocycle substituted with 0-3 R^{4b};
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, $C(=O)OR^{22}$, SR^{22}, OR^{14a}, OR^{22}, $NR^{21}R^{22}$, $S(=O)R^{22}$, $S(=O)_2R^{22}$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 haloalkyl-S-,

C_3-C_{10} carbocycle substituted with 0-3 R^{4b},
C_6-C_{10} aryl substituted with 0-3 R^{4b}, and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

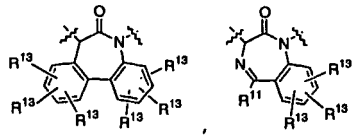
R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^5 is H;
C_1-C_6 alkyl substituted with 0-3 R^{5b};
C_2-C_6 alkenyl substituted with 0-3 R^{5b}; or
C_2-C_6 alkynyl substituted with 0-3 R^{5b};

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF_3, Cl, F, Br, I, =O;
C_3-C_6 carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Ring B is selected from: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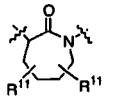
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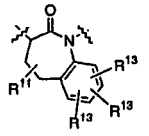

;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$, CF_3;
C_1-C_4 alkyl optionally substituted with 0-3 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; and wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, phenoxy, Cl, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_4 haloalkoxy;

W is a bond, $-CH_2-$, $-CH_2CH_2-$;

X is a bond;
phenyl substituted with 0-1 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-1 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-1 R^{Xb};

R^{Xb} is selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, methoxy, ethoxy, propoxy, and $-OCF_3$;

Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, or $-N(CH_2CH_3)-$;

Z is C_1-C_2 alkyl substituted with 1-2 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

R^{13}, at each occurrence, is independently selected from

H, OH, C_1-C_6 alkyl, C_1-C_4 alkoxy, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, C_1-C_4 alkyl, or C_2-C_4 alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, or C_1-C_4 alkyl;

R^{15}, at each occurrence, is independently selected from H, C_1-C_4 alkyl, and benzyl;

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-$S(=O)_2$-, and ethyl-$S(=O)_2$-;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl;

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl; and

R^{21} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl; and

R^{22} is methyl, ethyl, propyl, butyl, propenyl, butenyl, and propargyl.

10. A compound according to Claim 9 or a pharmaceutically acceptable salt or prodrug thereof wherein:

Q is $-CH_2R^4$, $-O-R^4$, or $-CH_2-NH-R^4$;

R^4 is C_1-C_6 alkyl substituted with 0-2 R^{4a},
C_2-C_6 alkenyl substituted with 0-2 R^{4a},
C_2-C_6 alkynyl substituted with 0-2 R^{4a}, or
C_3-C_6 cycloalkyl substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from is H, OH, F, Cl, Br, I, CN, $NR^{15}NR^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, OCF_3;
C_3-C_6 carbocycle substituted with 0-3 R^{4b},
phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$,
C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, and C_1-C_4 haloalkyl-S-;

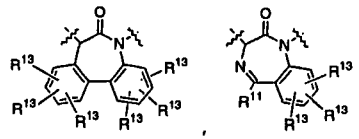
R^5 is H;
C_1-C_4 alkyl substituted with 0-1 R^{5b};
C_2-C_4 alkenyl substituted with 0-1 R^{5b}; or
C_2-C_4 alkynyl substituted with 0-1 R^{5b};

R^{5b}, at each occurrence, is independently selected from: H, methyl, ethyl, propyl, butyl, CF_3;
C_3-C_6 carbocycle substituted with 0-2 R^{5c};
phenyl substituted with 0-3 R^{5c}; and
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl,

thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, C_1-C_4 alkyl, C_1-C_3 alkoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

Ring B is selected from: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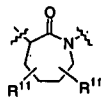
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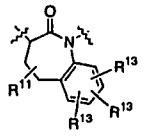

;

R^{11}, at each occurrence, is independently selected from H, =O, $NR^{18}R^{19}$;
C_1-C_4 alkyl optionally substituted with 0-3 R^{11a};
phenyl substituted with 0-3 R^{11b};
C_3-C_6 carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 3 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; and wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a}, at each occurrence, is independently selected from

H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, phenoxy, Cl, F, =O, $NR^{15}R^{16}$, CF_3, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1-C_2 haloalkyl, and C_1-C_2 haloalkoxy;

W is a bond or $-CH_2-$;

X is a bond;
phenyl substituted with 0-1 R^{Xb};
C_3-C_6 cycloalkyl substituted with 0-1 R^{Xb}; or
5 to 6 membered heterocycle substituted with 0-1 R^{Xb};

R^{Xb} is selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, methyl, ethyl, methoxy, ethoxy, and $-OCF_3$;

Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, $-N(CH_3)-$, or $-N(CH_2CH_3)-$;

Z is C_1-C_2 alkyl substituted with 1-2 R^{12a};
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-3 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
C_6-C_{10} aryl substituted with 0-4 R^{12b};
C_3-C_{10} carbocycle substituted with 0-4 R^{12b}; and
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered

heterocycle is substituted with 0-3 R^{12b}; and wherein said 5 to 10 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, tetrazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, isoxazolidinyl, benzotriazolyl, benzisoxazolyl, oxindolyl, benzoxazolinyl, quinolinyl, and isoquinolinyl;

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3, acetyl, SCH_3, $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, and $-OCF_3$;

R^{13}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, $NR^{15}R^{16}$, and CF_3;

R^{14} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R^{15}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl; and

R^{16}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl, benzyl, and phenethyl;

R^{18}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R^{19}, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl.

11. A compound, according to Claim 10, wherein:

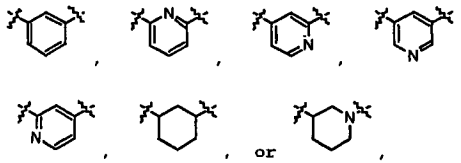
R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2NH_2$, $-CH_2N(CH_3)_2$, $-CH_2N(CH_2CH_3)_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, or $-CH_2CH_2$-cyclohexyl;

Q is $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH_2CH_2CH_2CH_2CH_3$, $-CH_2CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2$-cyclopropyl, $-CH_2$-cyclobutyl, $-CH_2$-cyclopentyl, $-CH_2$-cyclohexyl, $-CH_2CH_2$-cyclopropyl, $-CH_2CH_2$-cyclobutyl, $-CH_2CH_2$-cyclopentyl, $-CH_2CH_2$-cyclohexyl, $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$, $-OCH(CH_3)_2$, $-OCH_2CH_2CH_2CH_3$, $-OCH_2CH(CH_3)_2$, $-OCH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH_2CH_2CH_3$, $-OCH_2CH_2CH_2CH(CH_3)_2$, $-OCH_2CH_2CH_2CH_2CH(CH_3)_2$, $-OCH_2$-cyclopropyl, $-OCH_2$-cyclobutyl, $-OCH_2$-cyclopentyl, $-OCH_2$-cyclohexyl, $-OCH_2CH_2$-cyclopropyl, $-OCH_2CH_2$-cyclobutyl, $-OCH_2CH_2$-cyclopentyl, $-OCH_2CH_2$-cyclohexyl, $-CH_2OCH_2CH_3$, $-CH_2OCH_2CH_2CH_3$, $-CH_2$-$OCH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH_2CH_3$, $-CH_2OCH_2CH_2CH(CH_3)_2$, $-CH_2OCH_2CH_2CH_2CH(CH_3)_2$, $-CH_2O$-cyclopropyl, $-CH_2O$-cyclobutyl, $-CH_2O$-cyclopentyl, $-CH_2O$-cyclohexyl, $-CH_2OCH_2$-cyclopropyl, $-CH_2OCH_2$-cyclobutyl, $-CH_2OCH_2$-cyclopentyl, $-CH_2OCH_2$-cyclohexyl; $-CH_2(NH)CH_3$, $-CH_2(NH)CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH_3$, $-CH_2$-$(NH)CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH_2CH_3$, $-CH_2(NH)CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)CH_2CH_2CH_2CH(CH_3)_2$, $-CH_2(NH)$-cyclopropyl,

$-CH_2(NH)$-cyclobutyl, $-CH_2(NH)$-cyclopentyl, $-CH_2(NH)$-cyclohexyl, $-CH_2(NH)CH_2$-cyclopropyl, $-CH_2(NH)CH_2$-cyclobutyl, $-CH_2(NH)CH_2$-cyclopentyl, or $-CH_2(NH)CH_2$-cyclohexyl;

W is a bond or $-CH_2-$;

X is a bond;



Y is a bond, $-C(=O)-$, $-O-$, $-S-$, $-S(=O)-$, $-S(=O)_2-$, $-NH-$, or $-N(CH_3)-$,

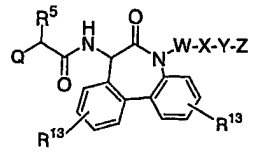
Z is phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl, 2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl, 2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl, 3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl, 2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl, 3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl, 3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl, 3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl, 4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl, 2-CF_3O-phenyl, 3-CF_3O-phenyl, 4-CF_3O-phenyl, furanyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl, 4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl, 1-benzimidazolyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, morpholino, N-piperinyl, phenyl-CH_2-, (2-F-phenyl)CH_2-, (3-F-phenyl)CH_2-, (4-F-phenyl)CH_2-, (2-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2, (4-Cl-phenyl)CH_2-, (2,3-diF-phenyl)CH_2-, (2,4-diF-phenyl)CH_2-, (2,5-diF-phenyl)CH_2-, (2,6-diF-phenyl)CH_2-, (3,4-diF-phenyl)CH_2-,

(3,5-diF-phenyl)CH_2-, (2,3-diCl-phenyl)CH_2-, (2,4-diCl-phenyl)CH_2-, (2,5-diCl-phenyl)CH_2-, (2,6-diCl-phenyl)CH_2-, (3,4-diCl-phenyl)CH_2-, (3,5-diCl-phenyl)CH_2-, (3-F-4-Cl-phenyl)CH_2-, (3-F-5-Cl-phenyl)CH_2-, (3-Cl-4-F-phenyl)CH_2-, (2-MeO-phenyl)CH_2-, (3-MeO-phenyl)CH_2-, (4-MeO-phenyl)CH_2-, (2-Me-phenyl)CH_2-, (3-Me-phenyl)CH_2-, (4-Me-phenyl)CH_2-, (2-MeS-phenyl)CH_2-, (3-MeS-phenyl)CH_2-, 4-MeS-phenyl)CH_2-, (2-CF_3O-phenyl)CH_2-, (3-CF_3O-phenyl)CH_2-, (4-CF_3O-phenyl)CH_2-, (furanyl)CH_2-,(thienyl)CH_2-, (pyridyl)CH_2-, (2-Me-pyridyl)CH_2-, (3-Me-pyridyl)CH_2-, (4-Me-pyridyl)CH_2-, (1-imidazolyl)CH_2-, (oxazolyl)CH_2-, (isoxazolyl)CH_2-, (1-benzimidazolyl)CH_2-, (cyclopropyl)CH_2-, (cyclobutyl)CH_2-, (cyclopentyl)CH_2-, (cyclohexyl)CH_2-, (morpholino)CH_2-, (N-pipridinyl)CH_2-, or (phenyl)$_2$CH-;

R^{11}, at each occurrence, is independently selected from H, =O, methyl, ethyl, phenyl, benzyl, phenethyl, 4-F-phenyl, (4-F-phenyl)CH_2-, (4-F-phenyl)CH_2CH_2-, 3-F-phenyl, (3-F-phenyl)CH_2-, (3-F-phenyl)CH_2CH_2-, 2-F-phenyl, (2-F-phenyl)CH_2-, (2-F-phenyl)CH_2CH_2-, 4-Cl-phenyl, (4-Cl-phenyl)CH_2-, (4-Cl-phenyl)CH_2CH_2-, 3-Cl-phenyl, (3-Cl-phenyl)CH_2-, (3-Cl-phenyl)CH_2CH_2-, 4-CH_3-phenyl, (4-CH_3-phenyl)CH_2-, (4-CH_3-phenyl)CH_2CH_2-, 3-CH_3-phenyl, (3-CH_3-phenyl)CH_2-, (3-CH_3-phenyl)CH_2CH_2-, 4-CF_3-phenyl, (4-CF_3-phenyl)CH_2-, (4-CF_3-phenyl)CH_2CH_2-, pyrid-2-yl, 4-F-pyrid-2-yl, 4-Cl-pyrid-2-yl, 4-CH_3-pyrid-2-yl, 4-CF_3-pyrid-2-yl, pyrid-3-yl, 4-F-pyrid-3-yl, 4-Cl-pyrid-3-yl, 4-CH_3-pyrid-3-yl, 4-CF_3-pyrid-3-yl, or pyrid-4-yl; and

R^{13}, at each occurrence, is independently selected from H, F, Cl, OH, -CH_3, -CH_2CH_3, -OCH_3, or -CF_3.

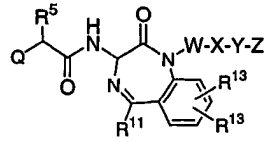
12. A compound according to one of Claims 4-11 of Formula (Ic):



(Ic)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

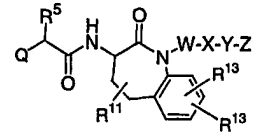
13. A compound according to one of Claims 4-11 of Formula (Id):



(Id)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

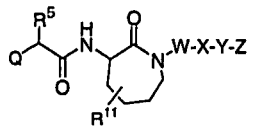
14. A compound according to one of Claims 4-11 of Formula (Ie):



(Ie)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

15. A compound according to one of Claims 4-11 of Formula (If):



(If)

or a stereoisomer, pharmaceutically acceptable salt or prodrug thereof.

16. A compound according to Claim 1, or a pharmaceutically acceptable salt or prodrug thereof, selected from:

(3*S*)-3-[(1-oxo-(2*S*)-2-cyclopropylmethyl-heptyl)]amino-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-propyloctyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-propylnonanyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-butyloctyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-(1-oxo-2-methyloctyl)amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-pentylheptanyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-propylpentyl)]amino-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

(3S)-3-[(1-oxo-2-methylpentyl)amino]-1-methyl- 5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one;

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-(pyridin-2-yl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one;

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-[4-methyl(pyridin-2-yl)]-2,3-dihydro-1H-1,4-benzodiazepin-2-one;

3-[1-oxo-2-(S)-cyclopropylmethyl-heptyl]amino-1-methyl-5-[4-trifluoromethyl(pyridin-2-yl)]-2,3-dihydro-1H-1,4-benzodiazepin-2-one;

3-[1-oxo-2-(S)-aminomethyl-heptyl]amino-1-methyl-(5-trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one;

3-[1-oxo-2-(S)-(dimethylamino)methyl-heptyl]amino-1-methyl-5-(trifluoromethyl-phenyl)-2,3-dihydro-1H-1,4-benzodiazepine-2-one; and

3-(3-isopentyloxy-2-(R)-methyl-1-oxo-propyl)amino-1-methyl-5-(trifluoromethyl)phneyl-2,3-dihydro-1H-1,4-benzodiazepin-2-one.

17. A compound according to Claim 1, or a pharmaceutically acceptable salt or prodrug thereof comprising:

(7S)-[(2S)-1-oxo-2-pentyloxy-4-methylpentyl]amino-5-methyl-5H,7H-dibenzo[b,d]azepin-6-one.

18. A pharmaceutical composition comprising a compound according to one of Claims 1-17 and a pharmaceutically acceptable carrier.

19. A method for the treatment of neurological disorders associated with β-amyloid production comprising administering to a host in need of such treatment a

therapeutically effective amount of a compound according to one of Claims 1-17.

20. A method for inhibiting γ-secretase activity comprising administering to a host in need of such inhibition a therapeutically effective amount of a compound according to one of Claims 1-17 that inhibits γ-secretase activity.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/11714

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D243/24 C07D401/04 C07D223/18 C07D223/12 C07D243/12
C07K05/06 A61K38/00 A61K31/55 A61K31/5513 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 16524 A (MERCK & CO INC) 1 October 1992 (1992-10-01) page 25 -page 26 page 61, line 9 -page 62, line 32 page 298 -page 320	1,18,19
X	US 5 817 658 A (CHANG PAUL I ET AL) 6 October 1998 (1998-10-06) tables I,II,III claim 1	1,18
X	US 5 633 251 A (CLAREMON DAVID A ET AL) 27 May 1997 (1997-05-27) examples 2,5,6,9,29,31 claims 1-10	1,18

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[X] Further documents are listed in the continuation of box C. [X] Patent family members are listed in annex.

* Special categories of cited documents :
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 August 2001	05/09/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Seitner, I

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 01/11714

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 14471 A (BALDWIN JOHN J ;ELLIOTT JASON M (US); LIVERTON NIGEL (US); MERCK &) 1 June 1995 (1995-06-01) tables I,II,V,VI page 26 examples 5-8,14,18,23,25,26,28-32 claims 1-6,11-15,20	1,18
X	EVANS B E ET AL: "METHODS FOR DRUG DISCOVERY: DEVELOPMENT OF POTENT, SELECTIVE, ORALLY EFFECTIVE CHOLECYSTOKININ ANTAGONISTS" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 31, no. 12, 1988, pages 2235-2246, XP000673671 ISSN: 0022-2623 example 31; table 1	1
P,X	WO 01 19797 A (DU PONT PHARM CO) 22 March 2001 (2001-03-22) examples 5,25A-C,31,36,38,33,40,41,118,42,43,45-47 claims 21-23 tables 3,4,5A-C,6,8	1,18-20
A	WO 98 35941 A (FUJIMOTO MASAFUMI ;SHIONOGI & CO (JP); HAGISHITA SANJI (JP); OKADA) 20 August 1998 (1998-08-20) table 10 examples 1-67 to 1-129	1,18-20
A	WO 99 32453 A (MCDANIEL STACEY L ;AUDIA JAMES E (US); ELAN PHARM INC (US); LILLY) 1 July 1999 (1999-07-01) table 1 page 3, line 5 -page 5, line 9	1,18-20
A	WO 95 35308 A (VERTEX PHARMA) 28 December 1995 (1995-12-28) page 1, line 4 -page 3, line 5 page 236, line 13 - line 14 examples 114A,106A,106B,106C,92	1,18-20

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

International Application No. PCT/US 01/11714

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-20 (all partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought. (Article 6 PCT).

Moreover, present claims 1-20 relate to compounds defined by reference to a desirable characteristic or property, namely to prodrugs of compounds of Formula (I) of claim 1.
The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

For these reasons it appears impossible to execute a meaningful search and/or to issue a complete search report over the whole breadth of the above mentioned claims.

The search and the report for those claims can only be considered complete the parts not pertaining to prodrugs and for:

-Compounds according to formula (I) of claim 1 for which
* W-X-Y-Z is hydrogen, C1-C8 alkyl substituted which 0-3 R12a, C2-C6 alkenyl substituted which 0-3 R12a, C2-C6 alkynyl substituted which 0-3 R12a, or C3-C10 carbocycle substituted which 0-3 R12b
* ring B is selected from definitions given in claim 3
* R6 is hydrogen
* R5 is any alkyl group according to definition in claim 7
* Q represents -CH2R4, -O-R4, or -CH2-NH-R4

-Pharmaceutical use and compositions of compounds of formula (I) of claim 1 according to claims 18-20.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/11714

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Form PCT/ISA/210 (patent family annex) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

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